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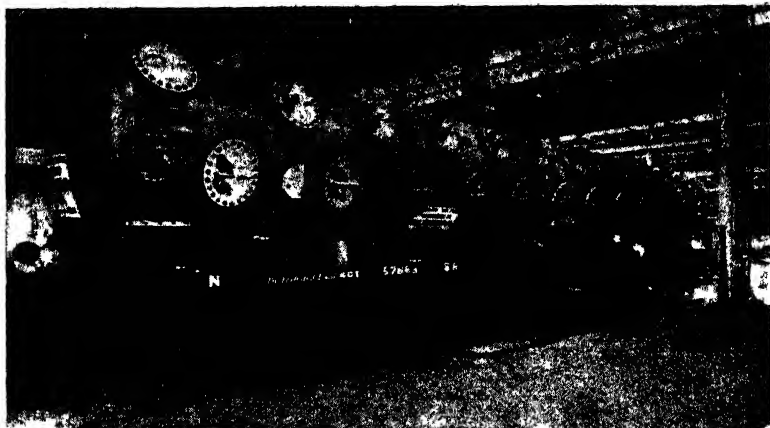
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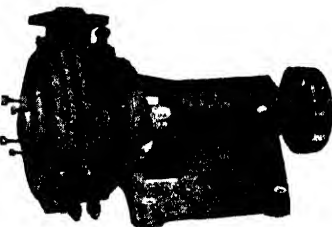
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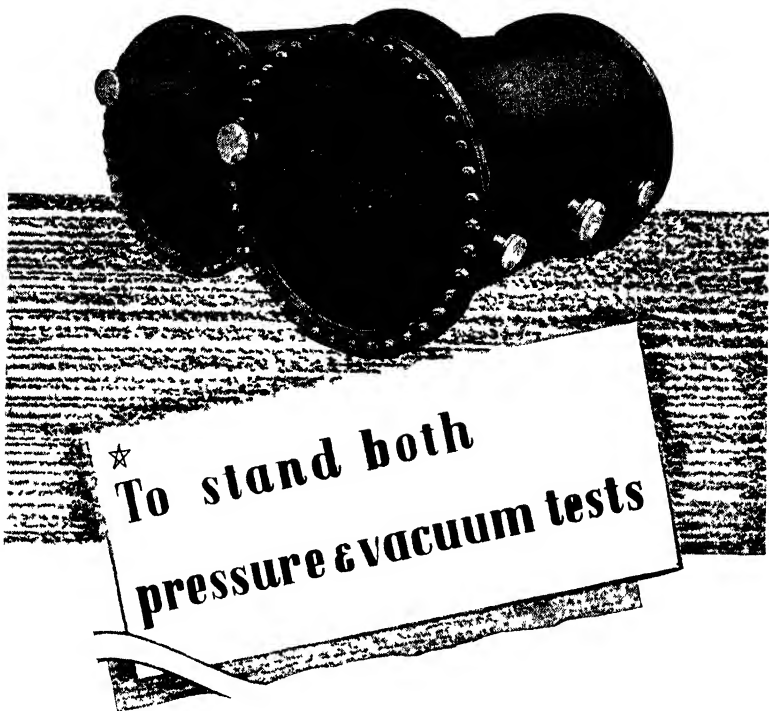
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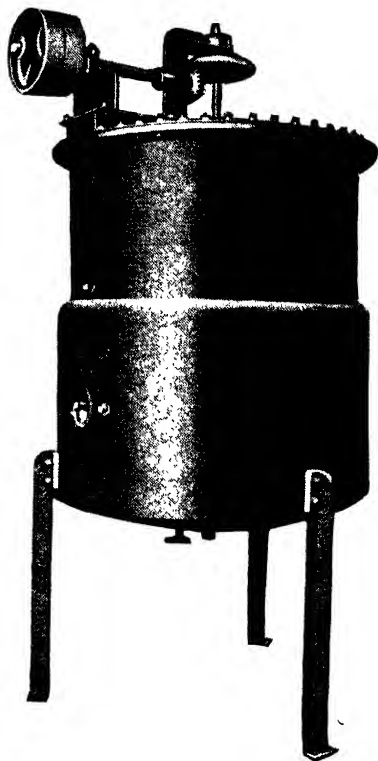
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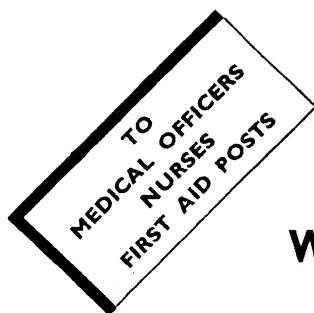
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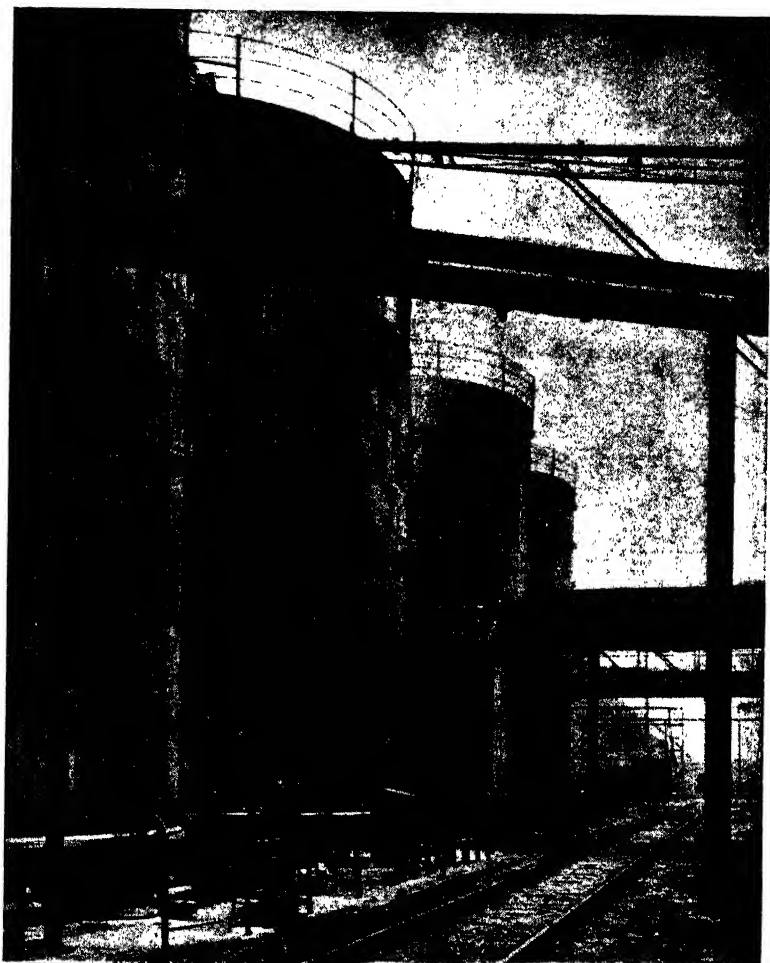
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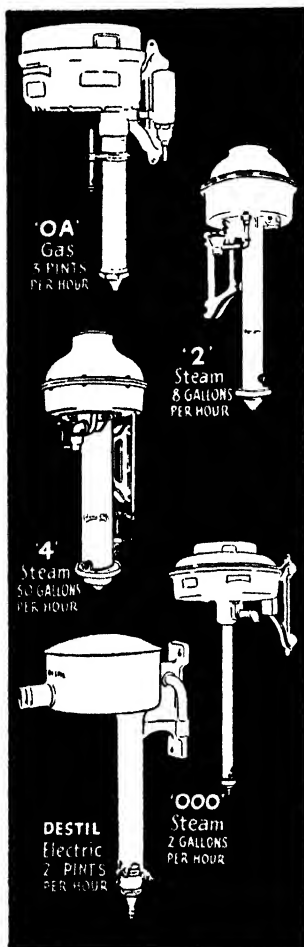


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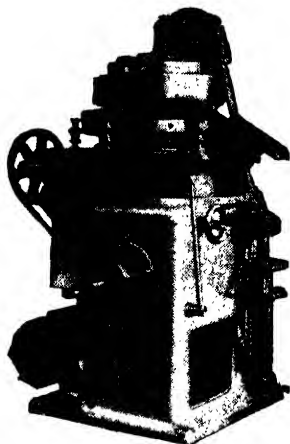
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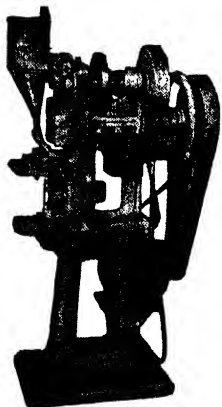
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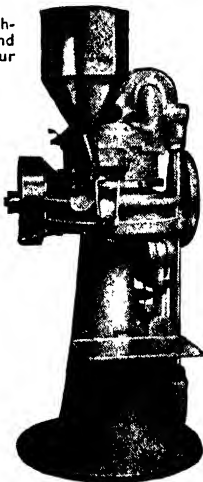
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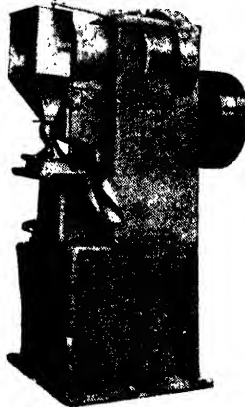
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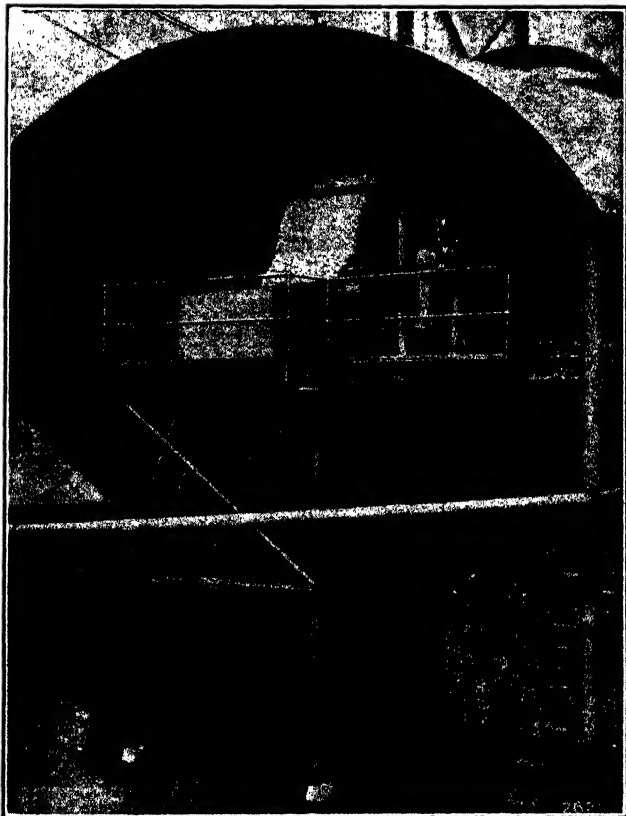
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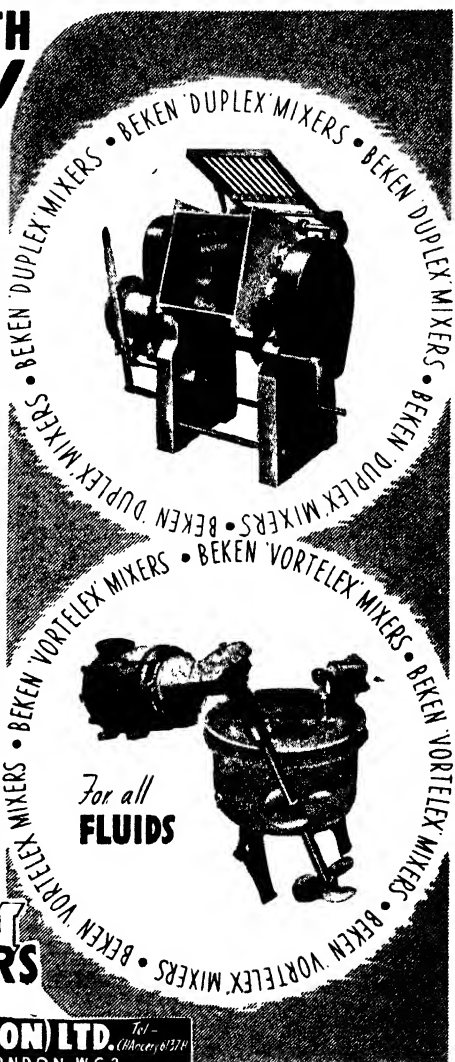
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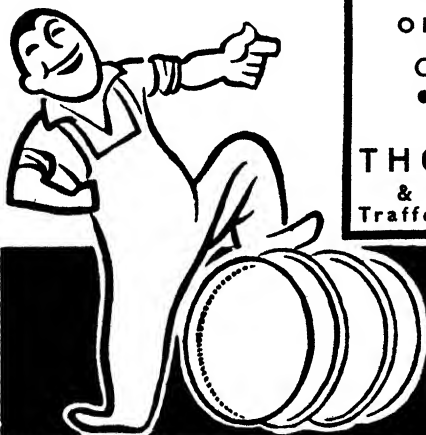
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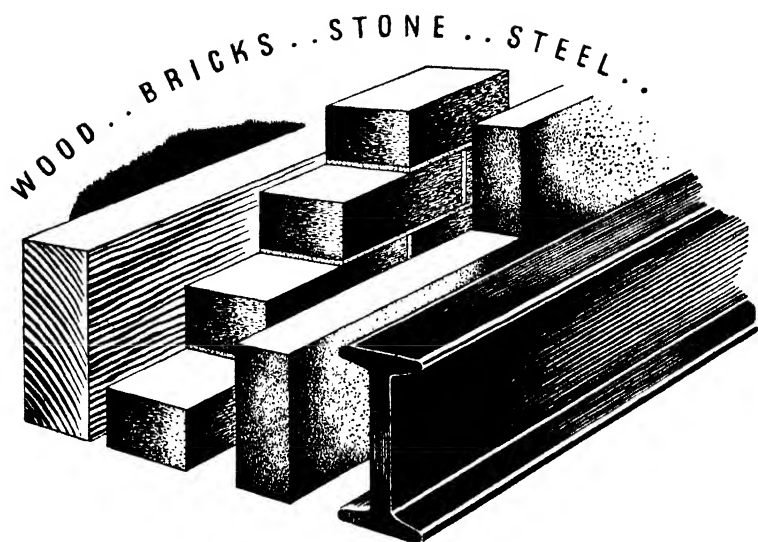
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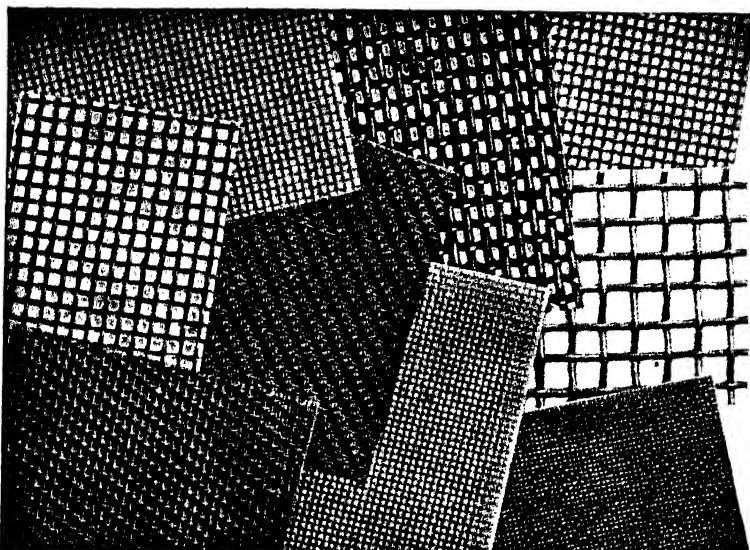
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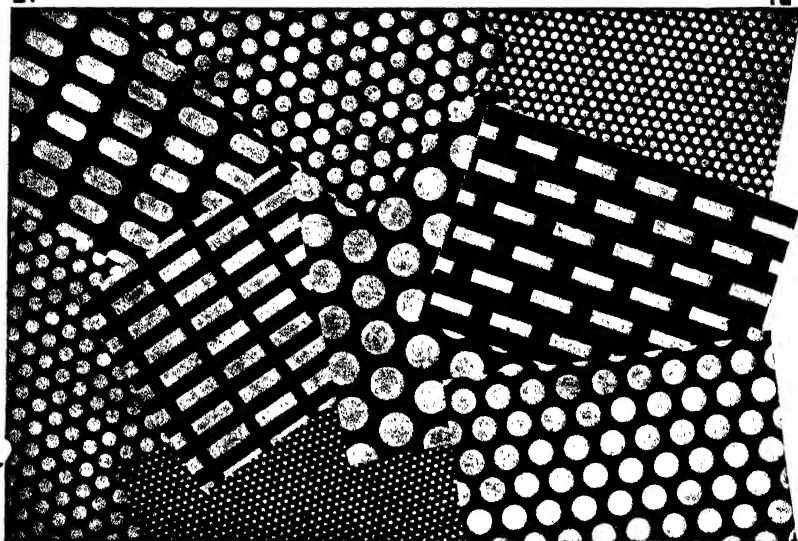
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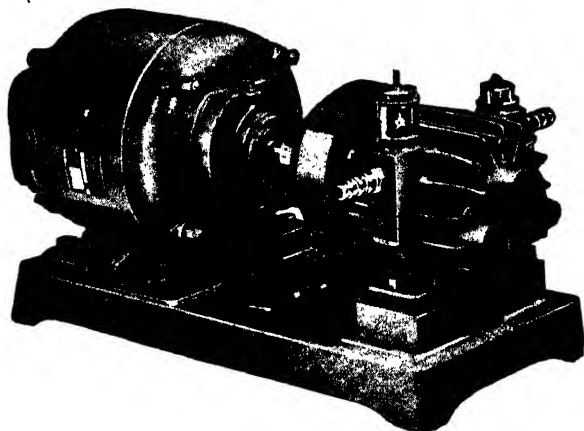
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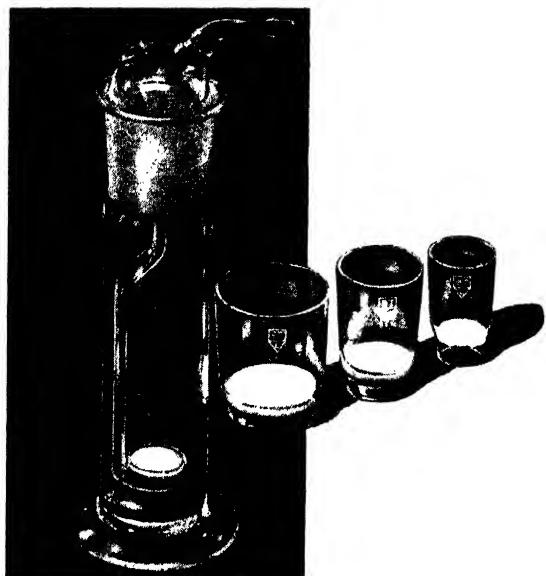
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ERRATUM.

VOL., 1940, 37.

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70 6* for " $121^{\circ} \pm 2^{\circ}$ " read " $112^{\circ} \pm 2^{\circ}$; see ref. 44, p. 1435."

* From bottom.

ANNUAL REPORTS ON THE PROGRESS OF CHEMISTRY.

GENERAL AND PHYSICAL CHEMISTRY.

1. INTRODUCTION.

OWING to the lack of recently published work in physical chemistry it is becoming increasing difficult to adhere to a planned scheme of articles over a short period of years. Any lack of balance in the present report is entirely due to this state of affairs.

Much attention is usually devoted to spectra as a means of determining the structure of molecules. In such surveys, however, there has been small mention of electronic absorption spectra in the ultra-violet. Although it is difficult to go deeply into the origin of the absorption bands in this region of the spectrum, yet there is much to be learned from an exact study of spectra of this type. R. A. Morton records recent advances in this field. Magnetic measurements provide yet another tool for investigation of molecular structure and reactions. The subject is a wide one and therefore W. R. Angus restricts his report exclusively to results from substances exhibiting diamagnetism. It is hoped in the future to deal with paramagnetism.

If two groups of atoms are joined together by a single bond, it is known that these groups may or may not rotate with respect to each other. The criterion for non-rotation has hitherto been the isolation of the two isomers. This condition only obtains when the energy required to rotate the group is much greater than kT . When that energy is only somewhat greater than kT , chemical methods are inapplicable. Here, however, specific heat measurements, coupled with observations on infra-red spectra, reveal phenomena which can only be explained if it is supposed that there is hindered rotation. H. W. Thompson reviews the subject in his report together with some additional infra-red work.

H. W. M.

2. ABSORPTION SPECTRA.

The present Report deals with absorption spectra as a part of physical chemistry, but the topic has such wide ramifications that a unified picture of the state of the subject is not easy to achieve in a small space. The applications of spectrophotometry to analytical and biochemical problems have been discussed elsewhere (see p. 26 for references).

In no field has improved experimentation given a greater reward than

in the study of absorption spectra. This is not the place to discuss the great advances which have been made in technique, but it is noteworthy that for at least 20 years the possession of adequate equipment has acted as a stimulus to the assimilation of theoretical ideas. The foundations for fundamental advances have been well laid; the need is now for better data, and, as will be seen in many of the researches reviewed below, the capacity to make use of such data is not lacking.

Notation.—If I_0 is the intensity of light of wave-length λ incident upon an absorbing medium of thickness d , and I the intensity of the emergent light, $\log I_0/I = E$ (extinction) $= kd$. Beer's law states that absorption is proportional to the number of molecules in the light path, i.e., $I = I_0 \cdot 10^{-\epsilon cd}$ where c is molar concentration (e.g., of an absorbing solute in a "transparent" solvent), d is thickness in cm., and ϵ is the molecular extinction coefficient. (Alternatively, $I = I_0 e^{-4\pi\kappa d/\lambda}$, $\kappa = 0.1832\epsilon c\lambda$, λ in cm.) The expression $^1 E_d^c$ stands for $\log I_0/I$ for a d -cm. layer of concentration c , and is useful as a way of describing an actual measurement, and for specifying the intensity of absorption of mixtures or substances of unknown molecular weight, in the form $E_{1\text{cm.}}^1\%$. An absorption band is usually described in terms of λ_{max} , or ν_{max} , ($\bar{\nu}_{\text{max}}$) and ϵ_{max} , i.e., the wave-length in Å. or millimicrons, $m\mu$, of maximum absorption, or the corresponding wave-number $1/\lambda$ cm.⁻¹ $= \bar{\nu}$ or frequency $c/\lambda = \nu^*$, and the molecular extinction coefficient at that wave-length. It is also desirable to note the half-width of a band, i.e., the distance in cm.⁻¹ between wave-numbers such that $\epsilon = \epsilon_{\text{max.}}/2$, and the band strength $\int \epsilon \cdot d\nu$.

The theoretical aspect of the intensity and width of an absorption band is discussed by N. G. Chako² and by Th. Förster.³ Let ν_j stand for the frequency of maximum absorption ϵ (for a band sufficiently distant from other bands) and γ_j a quantity measuring the damping and responsible for the width of the band, whilst f_j measures the strength; in classical theory f_j is the number of electrons per molecule producing the band, and in quantum theory it is a measure of the probability of the transition compared with that of the standard classical band. The sum of all the f_j 's is equal to the number of electrons. Most visible and ultra-violet bands are weak, i.e., the bands mainly responsible for the refractive index lie in the vacuum ultra-violet. From the theory of dispersion (e and m , charge and mass, respectively, of an electron)

$$2n^2k = \frac{e^2}{\pi m} N' \frac{f_j \gamma_j \nu}{(\nu_j^2 - \nu^2)^2 + \gamma_j^2 \nu^2}$$

and with $\epsilon = 4\pi nk/\lambda$ and $N' = N\mu$ (μ = molecules/c.c.)

$$\epsilon = \frac{2e^2}{cm} \frac{N}{n} \frac{f_j \gamma_j \nu^2}{(\nu_j^2 - \nu^2)^2 + \gamma_j^2 \nu^2}$$

¹ A. E. Gillam and R. A. Morton, *Proc. Roy. Soc.*, 1929, A, **124**, 609.

² *J. Chem. Physics*, 1934, **2**, 644.

³ *Z. Elektrochem.*, 1939, **45**, 551.

* $c = 3 \times 10^{10}$ cm./sec., velocity of light.

and if the band is narrow

$$\int \epsilon \cdot d\nu = \frac{\pi e^2}{cm\nu_j^2} \cdot \frac{N}{n} \cdot f_j, \text{ which is independent of } \gamma.$$

Further,
$$\epsilon_{\max.} = \frac{2e^2 N}{cm\nu} \cdot \frac{f_j}{\nu^2} \cdot \frac{1}{\gamma_j} \quad (\nu = \nu_j)$$

or
$$\gamma_j \cdot \epsilon_{\max.} = \frac{2}{\pi} \int \epsilon \cdot d\nu$$

and if γ were independent of ν throughout the band, the half-width (*i.e.*, distance between places where $\epsilon = \frac{1}{2}\epsilon_{\max.}$) is $\Delta\nu = 2\gamma$.

Numerically $\int \epsilon \cdot d\nu = 2.32 \times 10^8 \text{ cm.}^{-1}$, so with a value of *ca.* 2000 cm.^{-1} for the half-width, $\epsilon_{\max.} \sim 10^5$. An approximate upper limit of 100,000 for ϵ is not inconsistent with either quantum mechanics or general experience for a single electronic transition in a molecule. The absorption process implies that a molecule in its ground state E_0 (lowest energy) passes to excited states E_1, E_2 , etc., in accordance with $h\nu = E_1 - E_0$ by an electronic transition. Vibrations may also be excited, so that a more accurate relation is $h\nu = E_1 - E_0 + E_v$, where E_v is the vibrational energy.

Absorptive processes are of many different types. Instead of attempting a detailed exposition, it is proposed to select a number of representative recent studies with sufficient references to enable the reader to amplify the argument where it suffers from over-condensation.

Halogens.—The continuous absorption of chlorine⁴ has been studied over the range 18—709°, and analysis of the curves reveals a dual mechanism *A* ($\lambda_{\max.}$ 330 μ , $\epsilon_{\max.}$ 66) and *B* ($\lambda_{\max.}$ ~ 425 μ , $\epsilon_{\max.}$ ~ 1). *A* leads to dissociation into normal atoms ($^2P_{11}$), whereas *B* leads to one normal ($^2P_{11}$) and one excited (2P_1) atom. Similarly, bromine vapour exhibits composite absorption⁵ ($\lambda_{\max.}$ 415 and 495 μ) in the near ultra-violet and visible, but lacks an ultra-violet maximum shown near 250—300 μ in solution. Liquid bromine ($\lambda_{\max.}$ 405 μ , $\epsilon_{\max.}$ 350) also shows no ultra-violet maximum of this type,⁶ but the main band is more than twice as intense as in the vapour. In passing through a range of solvents from water to cyclohexane, $\lambda_{\max.}$ varies from 393 to 422 μ and $\epsilon_{\max.}$ from 164 (2N-sulphuric acid) to 360 (toluene). The effects of different solvents on different electronic transitions are quite marked.

The data on iodine are less difficult to interpret. Iodine molecules (vapour or violet solutions) give rise to two regions of selective absorption, the main one near 500 μ resulting in dissociation to one normal and one excited atom, and the other (near 732 μ) in two normal atoms.^{7, 8} The separation of these two bands (0.8 volt) reappears in the spectrum of iodine

⁴ R. G. Aickin and N. S. Bayliss, *Trans. Faraday Soc.*, 1937, **33**, 1332.

⁵ R. G. Aickin, N. S. Bayliss, and A. L. G. Rees, *Proc. Roy. Soc.*, 1939, *A*, **169**, 234; N. S. Bayliss, *ibid.*, 1937, *A*, **158**, 551; A. F. Acton, N. S. Bayliss, and R. G. Aickin, *J. Chem. Physics*, 1936, **4**, 474.

⁶ D. Porret, *Proc. Roy. Soc.*, 1937, *A*, **162**, 414.

⁷ C. B. Allsopp, *ibid.*, 1937, *A*, **158**, 167.

⁸ W. G. Brown, *Physical Rev.*, 1931, **38**, 1187.

adsorbed on calcium fluoride⁹ with very intense absorption characteristic of a very thin adsorbed layer (λ_{\max} , 345 and 284 $m\mu$). The large displacement (1.9 volts) is an indication of the change in binding energy on adsorption. Hydrated iodide ions I^- show twin maxima (λ 193.5, 226.2 $m\mu$; $\log \epsilon$ 4.13), and similarly spaced bands occur in alcoholic solutions of mercuric and cadmium iodides.¹⁰ In the simple alkyl iodides¹¹ the *A* process (λ_{\max} , 256 $m\mu$) leads to an excited iodine atom (2P_1) and an unexcited alkyl group, whereas the *B* process (λ_{\max} , 286.5 $m\mu$) liberates both in the unexcited state. The absorption of tri-iodides generally is characterised by two maxima resembling those of iodine adsorbed by calcium fluoride.

The original observation by T. M. Lowry¹² that the spectra of iodoform and potassium tri-iodide are very similar raised interesting issues beyond the scope of simple valency theories.

The results in Table I make it clear that the simultaneous production of iodine atoms in the normal and in the excited metastable state accounts

TABLE I.

Substance.	Solvent.	λ_{\max} , $m\mu$.	$\log \epsilon_{\max}$.	λ_{\max} , $m\mu$.	$\log \epsilon_{\max}$.
KI ₃	EtOH	355	3.9	290	3.9
CsI ₃	EtOH	360	4.46	290	4.6
	H ₂ O	352	3.3	290	3.44
CsI ₂ Br	EtOH	358	4.02	290	4.22
I ₂	(on CaF ₂) ca.	350	5.0	285	5.0
					(very thin layer)
TeMe ₂ I ₂	C ₆ H ₁₄	357	3.7	284	4.05
AsI ₃ ⁷	EtOH	356	4.21	294	4.34
	(vapour)	386	—	284	—
SbI ₃ ¹³	EtOH ¹⁷	357	4.07	292	4.20
	(vapour)	343	—	277	—
BiI ₃ ⁷	EtOH	356	4.02	294	4.19
	(vapour) ¹³	338.6	—	281	—
SnI ₄ ^{7, 14}	C ₆ H ₁₄	ca. 365	3.9	ca. 285	3.6
Cl ₄ ⁷	CCl ₄	386	—	304	—
PI ₃ ¹⁶	C ₆ H ₁₂	375	3.2	285	3.82
CHI ₃ ¹⁵	CCl ₄	351	3.31	306.5	3.20
	(vapour)	345	—	294	—

for absorptive processes. The occurrence and stability of interhalogen¹⁷ compounds in solution and also the phenomena of dichroism in iodine derivatives have been studied spectroscopically, as have the properties of hydrogen iodide and bromide.^{18, 19} In these compounds absorption is

⁹ J. H. de Boer, *Z. physikal. Chem.*, 1931, **B**, **14**, 163; 1933, **B**, **21**, 208.

¹⁰ E. Lederle, *ibid.*, 1930, **B**, **10**, 121.

¹¹ D. Porret and C. F. Goodeve, *Proc. Roy. Soc.*, 1938, **A**, **165**, 31.

¹² J., 1926, 622.

¹³ K. Butkow, *Z. Physik*, 1934, **90**, 81.

¹⁴ M. I. Grant, *Trans. Faraday Soc.*, 1935, **31**, 433.

¹⁵ K. E. Gibson and T. Iredale, *ibid.*, 1936, **32**, 571.

¹⁶ R. H. Potterill and O. J. Walker, *ibid.*, 1937, **33**, 363.

¹⁷ A. E. Gillam and R. A. Morton, *loc. cit.*; *Proc. Roy. Soc.*, 1931, **A**, **132**, 152;

A. E. Gillam, *Trans. Faraday Soc.*, 1933, **29**, 1132.

¹⁸ C. F. Goodeve and A. W. C. Taylor, *Proc. Roy. Soc.*, 1935, **A**, **152**, 221; 1936, **A**, **154**, 181.

¹⁹ P. Fink and C. F. Goodeve, *ibid.*, 1937, **A**, **163**, 592.

localised in one part of the molecule, but the position of the band (*i.e.*, size of $h\nu$) may be affected by the presence of atoms or groups which disturb the electronic levels. This is in sharp contrast with the data for mesomeric systems, which will be referred to later.

Departures from Beer's law are usually a clue to some significant change, a simple example being sulphur dioxide in water.²⁰ An absorption band with λ_{\max} . 275 m μ shows $\log \epsilon_{\max}$. 1.82 at 0.004M, 2.2 at 0.04 and 0.4M, and 2.4 at 0.1M. The system consists of $\text{SO}_2, \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{SO}_3 \rightleftharpoons \text{H}^+ + \text{HSO}_3^-$, but HSO_3^- and H_2SO_3 make negligible contributions to the absorption. The absorbing entity is $\text{SO}_2, \text{H}_2\text{O}$, and when the equilibria are elucidated, constant ϵ values for this substance can be calculated. In pure hexane, sulphur dioxide exists unsolvated and Beer's law is valid (λ_{\max} . 290 m μ , $\log \epsilon_{\max}$. 2.4).

Nitrous acid (freshly prepared) exhibits a main maximum at 365 m μ with vibrational fine structure (narrow bands with a constant frequency difference of $\Delta \text{ cm}^{-1}$ 1000).²¹ Similar absorption appears in β -octyl nitrite²² and in methyl and ethyl nitrite,²³ and the vapour of nitrous acid²⁴ shows $\Delta \text{ cm}^{-1}$ 1000 and 250 (vibration of O—N=O group in an excited state). A maximum near 230 m μ in octyl nitrite corresponds with an electron-affinity spectrum.²⁵

The NO_2^- ion (sodium nitrite in sodium hydroxide) shows λ_{\max} . 353.5 m μ , and crystalline sodium and potassium nitrite at -250° ²⁶ show absorption in the same region with well-resolved vibrational bands ($\Delta \text{ cm}^{-1}$ 600) although barium nitrite crystals show no such bands. An inflexion near 287 m μ is possibly indicative of a second electronic excitation. Nitromethane shows a different weak band (λ_{\max} . 270 m μ , $\log \epsilon_{\max}$. 1.16) sharply illustrating the effect of an alternative structural arrangement.

The NO_3^- ion shows a strong band (λ_{\max} . 193.6 m μ , ϵ_{\max} . 12,000) and a weak band (λ_{\max} . 302 m μ , ϵ 6.4),²⁷ the latter due possibly to a forbidden transition occurring only when coupled with vibrational frequencies. In solutions the absorption is diffuse, probably as a result of an intermolecular Stark effect. Very definite evidence of vibrational frequencies ($\Delta \text{ cm}^{-1}$ 800) is obtained in the spectra of crystalline nitrates at -250° (potassium nitrate 350 and 750 cm^{-1}). The effects of interionic forces are shown in the displacements suffered by the NO_3^- band :

Dilute solutions.	Crystals.			Temp.
	KNO_3 .	NaNO_3 .	$\text{Ba}(\text{NO}_3)_2$.	
302	304	291.5	277.5 m μ .	Room temp.
	307	287	272.5	-250°

²⁰ H. Ley and E. König, *Z. physikal. Chem.*, 1938, B, **41**, 365.

²¹ G. Kortum, *ibid.*, 1939, B, **43**, 418.

²² W. Kuhn and H. L. Lehmann, *ibid.*, 1932, B, **18**, 32.

²³ G. H. Purkis and H. W. Thompson, *Trans. Faraday Soc.*, 1936, **32**, 1466.

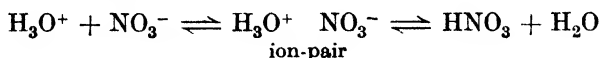
²⁴ E. H. Melvin and O. R. Wulf, *J. Chem. Physics*, 1935, **3**, 753.

²⁵ H. W. Thompson, *ibid.*, 1939, **7**, 136.

²⁶ H. Schaumann, *Z. Physik*, 1932, **76**, 106.

²⁷ R. A. Morton and R. W. Riding, *Proc. Roy. Soc.*, 1927, A, **113**, 717.

Departures from Beer's law occur in concentrated solutions owing probably to formation of ion-pairs.²⁸ 15N-Nitric acid shows weak selective absorption near 265 m μ , and a similar curve occurs with 0.15N-acid in the presence of 9.1N-perchloric acid, which is itself transparent. Nitric acid in pure hexane, however, shows end absorption (inflexion 280 m μ) similar to that of ethyl nitrate. The equilibria



appear to cover all aqueous solutions, the concentration of homopolar molecules being at most *ca.* 10^{-3} .

The MnO_4^- ion gives rise to groups of equidistant narrow bands²⁹ shown by solutions and by crystals. The solution spectra commence near 370 m μ and extend to the region near 600 m μ : $1/\lambda = 17520 + 747n \text{ cm}^{-1}$ ($n = 0 \dots 8$). In ethyl acetate the separation is 785 cm^{-1} . Various pure permanganates have been studied at low temperatures in the solid state:³⁰

	First principal maximum, cm^{-1} .	$\Delta\bar{\nu}$.	<i>H</i> (half-width).
KMnO_4	17632	774	200
RbMnO_4	17875	768	170
CsMnO_4	18125	757	160
NMe_4MnO_4	17622	756	110
BaMnO_4	17571	772	220

Dilute mixed crystals $\text{K}(\text{Cl},\text{Mn})\text{O}_4$ possess rhombic symmetry and at low temperatures exhibit three principal spectra in which the light vibrates parallel to the *a*, *b*, and *c* axes:

$$\begin{aligned}\bar{\nu} &= 18051 + n 763 + m 273 \parallel a \\ &18043 + n 768 + m 310 \parallel b \\ &18049 + n 767 + m 286 \parallel c\end{aligned}$$

The bands become sharper as the temperature falls; *e.g.*, the half-width is 130 cm^{-1} at 150° K., 70 cm^{-1} at 83° K., and 35 cm^{-1} at 20° K. Sodium perchlorate possesses a different crystal structure from the potassium, rubidium, or caesium salt, and the absorption of $\text{Na}(\text{Cl},\text{Mn})\text{O}_4$ mixed crystals depends markedly on crystal orientation: $\Delta \text{cm}^{-1} \parallel a$ 718, $\parallel b$ 796, $\parallel c$ much less intense, ill-defined absorption. Absorption by $\text{NH}_4(\text{Cl},\text{Mn})\text{O}_4$ is less sharp than that of $\text{NMe}_4(\text{Cl},\text{Mn})\text{O}_4$, and hydrated crystals give poorly defined bands in many cases. The hexagonal crystals like $\text{LiClO}_4 \cdot 3\text{H}_2\text{O}$ and $\text{Ba}(\text{ClO}_4)_2 \cdot 3\text{H}_2\text{O}$ exhibit very sharp bands (H 30 cm^{-1}) for the ordinary ray $\perp c$, whereas resolution is feeble or lacking for the extraordinary ray. The term disturbance due to water of crystallisation is thus confined to one direction. In $\text{K}(\text{Cl},\text{Mn})\text{O}_4$ a second electronic transition gives rise to a very weak sequence of bands near 14570 cm^{-1} ($\Delta\bar{\nu}$ variable, *ca.* 800; H 40—90 cm^{-1} depending on direction). The MnO_4^- band system in sodium perchlorate shows several electronic transitions, depending to a striking

²⁸ H. v. Halban and J. Eisenbrand, *Z. physikal. Chem.*, 1928, **A**, 132, 433.

²⁹ A. M. Taylor, *Trans. Faraday Soc.*, 1929, **25**, 860.

³⁰ J. Teltow, *Z. physikal. Chem.*, 1938, **B**, 40, 397; 1939, **B**, 43, 198.

extent on direction. The crystal field shows specially great anisotropy, and suitable crystals exhibit dichroism, changing colour in polarised light between red and deep violet. An ultra-violet system (with ϵ one-tenth that of the main system) near $277 \text{ m}\mu$ ($\Delta \text{ cm.}^{-1} 756$) occurs even in solutions. This kind of electronic band spectrum with a large number of equidistant bands is characteristic of totally symmetrical vibrations (expansion and contraction of the MnO_4^- tetrahedron). Osmium tetroxide, OsO_4 , is an example of a similar state of affairs in a free molecule (3 ultra-violet systems : $\Delta\bar{\nu}$ 811, 835, 832 cm.^{-1}).

The MnO_4^{--} and CrO_4^{--} ions in $\text{K}_2(\text{S,Cr,Mn})\text{O}_4$ exhibit similarly spaced maxima, but no resolution can be detected with the VO_4^{---} ion. The crystal $\text{K}(\text{Cl,Mn})\text{O}_4$ with a moderate manganese concentration shows a single very sharp line at $\bar{\nu}$ 14446 ($H = 8 \text{ cm.}^{-1}$) in the $\parallel b$ direction, but this is lacking altogether in the $\parallel a$ direction. The line is a pure electronic transition which can only occur in combination with a vibration. In some instances whole band systems are missing. The MnO_4^- ion possesses an incomplete shell, well shielded by valency electrons : it is the tetrahedral ions of the transition elements which show selective absorption, unlike the transparent ClO_4^- , SO_4^{--} , and PO_4^{---} ions.

The $\text{Co}(\text{Hal})_4^{--}$ ions are not altogether dissimilar, but the position is not quite so clear.³¹⁻³⁷

New effects appear with neodymium salt spectra at low temperatures.³⁸ Electronic transitions in the well-shielded incomplete neodymium shell are shown, in $\text{NdCl}_3 \cdot 6\text{H}_2\text{O}$ crystals at the temperature of liquid hydrogen, to couple with internal vibrational frequencies of the molecules as well as with various modes of vibration of the lattice. This is shown by the recurrence of certain intense groups, the intervals between the parent pattern and the repetitions conforming frequently with well-known vibrational frequencies : ³⁹

Substance.	$\Delta\bar{\nu}$, cm.^{-1} .	$\Delta\bar{\nu}$ (Raman), obs.
$3\text{Zn}(\text{NO}_3)_2 \cdot 2\text{Nd}(\text{NO}_3)_3 \cdot 24\text{H}_2\text{O}$	(a) 716, 746	725
	(b) 1046, 1051	1055
	(c) 1310	1370
$\text{Nd}_2(\text{SO}_4)_3 \cdot 8\text{H}_2\text{O}$	(a) 995, 1011	990
	1342, 1120	1125
	1640	

The chloride and bromate with ordinary water of crystallisation also show $\Delta\bar{\nu}$ 1640 and 1650. With heavy water $\Delta\bar{\nu}$ values of 1199 and 1431 cm.^{-1} (bromate) and 1238 and 1481 cm.^{-1} (chloride) are recorded. From other

³¹ W. R. Brode, *Proc. Roy. Soc.*, 1928, A, **118**, 286; *J. Amer. Chem. Soc.*, 1931, **53**, 2457.

³² W. R. Brode and R. A. Morton, *Proc. Roy. Soc.*, 1928, A, **120**, 21.

³³ A. v. Kiss and M. Gerendás, *Z. physikal. Chem.*, 1937, A, **180**, 117.

³⁴ W. Feitknecht, *Helv. Chim. Acta*, 1937, **20**, 659.

³⁵ O. R. Howell and A. Jackson, *Proc. Roy. Soc.*, 1933, A, **142**, 587.

³⁶ R. J. Macwalter and S. Barratt, *J.*, 1934, 517.

³⁷ P. Job, *Ann. Chim.*, 1936, **6**, 97.

³⁸ H. Ewald, *Ann. Physik*, 1939, [v], **34**, 209.

³⁹ K. H. Hellwege, *Z. Physik*, 1939, **113**, 192.

independent work the inner vibrations to be expected are 1615 cm^{-1} or 1220 and 1460 cm^{-1} respectively.⁴⁰ Smaller intervals are associated with lattice vibrations.

Crystals of europium salts homologous with those of neodymium possess such sharp absorption spectra⁴¹⁻⁴⁶ that phenomena similar to those recorded at very low temperatures can be studied at room temperature. Changes in the environment of Eu^{+++} ions bring about alterations in the structure of the absorption spectrum. Thus EuCl_3 in water to which potassium nitrate is added exhibits the structures shown in $\text{Eu}(\text{NO}_3)_3$ as well as EuCl_3 .

The spectra of europium salts in alcohol differ from those shown by aqueous solutions. In a mixed solvent both spectra are shown with relative intensities which vary according to the proportions of the components. Repetitions of prominent patterns enable lattice vibrations to be evaluated, and in some cases a given electronic level of an ion in an electrostatic field is decomposed in strict accordance with theory into a number of sub-levels.

The interpretation of absorption spectra is rooted in classical dispersion theory, it comes to flower in the quantum-mechanics of diatomic molecules, and is reaching fruition with larger molecules. Simple saturated hydrocarbons like methane and ethane exhibit selective absorption^{47, 48} in the vacuum ultra-violet only (methane, λ_{max} , $120\text{--}130\text{ m}\mu$). Replacement of hydrogen by alkyl groups brings about progressive displacements towards longer wave-lengths (*n*-hexane, λ_{max} , *ca.* $153\text{ m}\mu$).⁴⁹ If absorption occurs at wave-lengths $>200\text{ m}\mu$, the presence of a double bond is indicated.

Absorption by ethylene begins near $175\text{ m}\mu$, and following a well-defined pattern, extends to $160\text{ m}\mu$, with additional bands near 139 and $129\text{ m}\mu$. The separate ν_0 values fit into a Rydberg formula and converge to an ionisation potential of 10.45 v. ; ^{50, 51}

$$\text{C}_2\text{H}_4 \nu_0^{(n)} = 84,750 - R/(n + 0.91)^2; n = 2, 3, 4, \text{etc.}$$

$$\text{C}_2\text{D}_4 \nu_0^{(n)} = 84,850 - R/(n + 0.92)^2; n = 2, 3, 4, \text{etc.}$$

The absorption bands (and ionisation potentials) refer respectively to excitation and removal of a " π " electron (see p. 15) from the double bond. Electrons of the $[\sigma]^2$ single C-C or C-H links need much higher frequencies for ionisation.

The vibrational structure, $\text{C}_2\text{H}_4 \Delta\text{ cm}^{-1}$ 1370 , $\text{C}_2\text{D}_4 \Delta\text{ cm}^{-1}$ 1290 , corre-

⁴⁰ L. Kellner, *Proc. Roy. Soc.*, 1937, **A**, **159**, 414.

⁴¹ S. Freed and S. I. Weissmann, *J. Chem. Physics*, 1938, **6**, 297.

⁴² S. Freed and H. F. Jacobson, *ibid.*, p. 654.

⁴³ S. Freed, S. I. Weissmann, F. E. Fortress, and H. F. Jacobson, *ibid.*, 1939, **7**, 824.

⁴⁴ S. I. Weissmann and S. Freed, *ibid.*, 1940, **8**, 227, 878.

⁴⁵ S. Freed, S. I. Weissmann, and F. E. Fortress, *J. Amer. Chem. Soc.*, 1941, **63**, 1079.

⁴⁶ F. H. Spedding, C. C. Moss, and R. C. Waller, *J. Chem. Physics*, 1940, **8**, 908.

⁴⁷ W. Groth, *Z. Elektrochem.*, 1939, **45**, 262.

⁴⁸ E. P. Carr and M. K. Walker, *J. Chem. Physics*, 1936, **4**, 751.

⁴⁹ E. P. Carr and H. Stucklen, *ibid.*, p. 760; *Z. physikal. Chem.*, 1934, **B**, **5**, 57; *J. Amer. Chem. Soc.*, 1937, **59**, 2138; *J. Chem. Physics*, 1938, **6**, 55.

⁵⁰ W. C. Price and W. T. Tuttle, *Proc. Roy. Soc.*, 1940, **A**, **174**, 207.

⁵¹ W. C. Price and A. D. Walsh, *ibid.*, p. 220.

sponds with the totally symmetrical valency frequency of the double bond, which in the ground states is either C_2H_4 $\Delta \text{ cm.}^{-1}$ 1623, or C_2D_4 $\Delta \text{ cm.}^{-1}$ 1515. The change in frequency resulting from isotopic substitution is in accord with expectations: $1370/1290 = 1.062$; $[16(\text{CD}_2)/14(\text{CH}_2)]^\dagger = 1.069$. Bands near $170 \text{ m}\mu$ appear in pairs, $\Delta \text{ cm.}^{-1}$ 470 and 300 for C_2H_4 and C_2D_4 respectively. The mass factor $(\text{D}/\text{H})^\dagger = 1.41$ is not very different from $470/300 = 1.57$; probably the CH_2 groups twist about the double bond.

The spectrum of butadiene is very important because this substance affords the simplest example of resonance between conjugated double bonds. The first strong absorption ($217 \text{ m}\mu$) is a progression of four diffuse bands, $\Delta 1440 \text{ cm.}^{-1}$ (isoprene, $221 \text{ m}\mu$, $\Delta 1450 \text{ cm.}^{-1}$). The symmetrical $\text{C}=\text{C}$ valency vibration (1634 cm.^{-1} in the ground state) is reduced a little by the excitation. Other electronic states are shown at higher frequencies, and twisting vibrations (pairs, $\Delta 350 \text{ cm.}^{-1}$) are recorded. Below $152 \text{ m}\mu$ vibrationless electronic transitions lead as before to the ionisation potential (9.02 v.):

$$\begin{aligned} \nu_0^{(n)} &= 73115 - R/(n + 0.90)^2; \quad n = 2, 3, 4, \text{ etc.} \\ &= 73006 - R/(n + 0.50)^2; \quad n = 3, 4, 5, \text{ etc.} \end{aligned}$$

With alkyl substitution, simple inductive effects diminish the ionisation potential. The absence of vibrational bands in the Rydberg transitions is a direct result of resonance; the removal of an electron shared between two bonds having a reduced effect on each.

The main absorption of the $\text{C}=\text{O}$ group also falls in the Schumann region ($<200 \text{ m}\mu$) and so also does that of the carboxyl group.⁵²⁻⁵⁴

Mesomerism in conjugated compounds is now accepted as a fact of major significance. Molecular resonance in polyene and aromatic hydrocarbons has been treated with success as a theorem in wave-mechanics⁵⁵⁻⁵⁹ leading to the calculation of $\text{C}-\text{C}$ distances and of colour. The only experimental parameter needed (α or J) may be evaluated from heats of hydrogenation.

Those dealing with wave-mechanics distinguish between localised electron pairs responsible for directed valency (interaction of σ electrons) and π electrons.⁶⁰⁻⁶² These "mobile electrons" (Lennard-Jones), "electrons of the second kind" (Hückel),⁶³ are not strictly localised and in planar molecules are antisymmetrical to the plane of the $\text{C}-\text{C}$ links, and cannot be paired according to their spins in a unique way to fit an ordinary structure.

⁵² W. M. Evans and W. C. Price, *Nature*, 1937, **139**, 630.

⁵³ A. B. F. Duncan, *J. Chem. Physics*, 1936, **3**, 131.

⁵⁴ V. R. Ells, *J. Amer. Chem. Soc.*, 1938, **60**, 1864.

⁵⁵ J. E. Lennard-Jones, *Proc. Roy. Soc.*, 1937, *A*, **158**, 280.

⁵⁶ J. E. Lennard-Jones and J. Turkevich, *ibid.*, p. 297.

⁵⁷ W. G. Penney, *ibid.*, p. 306.

⁵⁸ A. L. Sklar, *J. Chem. Physics*, 1937, **5**, 689.

⁵⁹ Th. Förster, *Z. physikal. Chem.*, 1938, *B*, **41**, 304; *Z. Elektrochem.*, 1939, **45**, 548.

⁶⁰ J. H. van Vleck and A. Sherman, *Rev. Mod. Physics*, 1935, **7**, 237.

⁶¹ L. Pauling, *J. Amer. Chem. Soc.*, 1931, **53**, 1367; *J. Chem. Physics*, 1933, **1**, 280.

⁶² J. C. Slater, *Physical Rev.*, 1931, **37**, 481; **38**, 1109.

⁶³ E. Hückel, *Z. Elektrochem.*, 1937, **43**, 752, 827; J. E. Lennard-Jones, *loc. cit.*

Such electrons cause links to become intermediate in distance between isolated double bonds and single bonds. Benzene is treated as a six-electron system with spin degeneracy only, and the single exchange integral between adjacent carbon atoms is α . Two electrons present on adjacent atoms lower the energy of a structure (by forbidding resonance) by $-\alpha$ (α is negative) if the electrons are paired to form a bond, and raise the energy by $-\frac{1}{2}\alpha$ if they are not paired. Thus a Kekulé form of benzene has an energy lowering of $(3\alpha - \frac{3}{2}\alpha) = 1.5\alpha$. In the result for benzene, 2.6α represents the normal state.

	Total energy.	Resonance energy.
Single Kekulé structure	1.5 α	0
Resonance between two Kekulé structures	2.4 α	0.9 α
Resonance between all 5 canonical structures ...	2.605 α	1.105 α

From heats of hydrogenation,⁶⁴ Sklar evaluates α as 1.92 v. (44 kg.-cals./mol.). The location of selective absorption can then be calculated :

Molecule.	Excitation energies.*	Wave length of first absorption region, in μ :	
		calc.	obs.
Benzene	2.40 α	245	255
Naphthalene ...	1.97 α (3.34 α)	295	275
Anthracene.....	1.60 α (3.0 α , 3.8 α)	365	370
Naphthacene ...	1.31 α (2.62 α , 3.56 α , 4.07 α)	450	460
Pentacene	1.08 α (2.2 α , 3.1 α , 4.0 α , 4.2 α)	545	580
Phenanthrene	1.94 α (. . .)	300	295
Pyrene	1.70 α (. . .)	345	330

* Approximate higher excitation states in parentheses.⁵⁹

By plotting $\Delta E/\alpha$ against λ , it appears that $\alpha = 2.11$ v. (49 kg.-cals./mol.), in good agreement with Sklar's result in view of the fact that the calculations are a first approximation.

An important series of papers⁶⁵⁻⁶⁸ on the highly selective absorption of polyenes, $R_1[CH:CH]_nR_2$ gives results agreeing with the concept of mobile electrons.

R_1	CH_3	Furyl	Ph	CH_3
R_2	CHO or	CHO or	Ph	CH_3
	CO_2H	CO_2H		
n	1, 2, 3, 4	0, 1, 2, 3	1, 2 . . . 7, 11, 15	1, 2 . . . 6

It being assumed⁶⁹ that the system of $-CH=CH-$ oscillators can be replaced by a single oscillator with the same coefficient of restoring force k , and mass proportional to n , it is shown that the energy levels for an oscillator of mass nm are given by $W_v = (v + \frac{1}{2})h\nu_0$ ($v = 0$ to $v = 1$) and $2\pi\nu_0 =$

⁶⁴ G. B. Kistiakowsky, J. R. Ruhoff, H. A. Smith, and W. E. Vaughan, *J. Amer. Chem. Soc.*, 1936, **58**, 146.

⁶⁵ K. W. Hausser, R. Kuhn, A. Smakula, and K. H. Kreuchen, *Z. physikal. Chem.*, 1935, *B*, **29**, 363.

⁶⁶ K. W. Hausser, R. Kuhn, and A. Smakula, *ibid.*, p. 384.

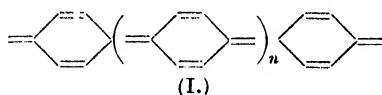
⁶⁷ K. W. Hausser, R. Kuhn, and G. Seitz, *ibid.*, p. 391.

⁶⁸ K. W. Hausser, R. Kuhn, and E. Kuhn, *ibid.*, p. 417.

⁶⁹ Cf. G. N. Lewis and M. Calvin, *Chem. Reviews*, 1939, **25**, 289.

$\sqrt{k/nm}$ (ν_0 , the first absorption band). Hence $\lambda_0 = 2\pi c/\sqrt{k/nm}$ or $\lambda_0^2 = 4\pi^2 c^2 nm/k$, i.e., $\lambda_0^2 = k'n$. On plotting λ_0^2 against n , for the diphenyl polyenes, a very good straight line is obtained cutting the n axis at -4.7 , so that on this basis each Ph equals 2.35 double bonds. The next higher vibrational level ($\Delta v = 2$) involves increasing anharmonicity and the levels come closer as v increases. The carotenoids show two well-marked regions of selective absorption (e.g., β -carotene, ca. 477 $m\mu$ and 270 $m\mu$; λ_1, λ_2).⁷⁰ The ratio λ_1/λ_2 is approximately constant in this class of compound at 1.7—1.85. This type of second-order band may be fairly common, but easily obscured by absorption due to a part of the molecule rather than the entire resonance system.⁶⁹

Similar relationships with polymethin dyes (pseudoisocyanine, isocyanine, and cyanine types),⁵⁹ conjugated azo-dyes,⁷¹ etc., fit in with the idea of resonating whole molecules. The p -polyphenyls (I) exhibit some approach towards double-bond character^{72, 73} for the internuclear link, but the m -series



is quite different:

Solvent: CHCl ₃ .			<i>m</i> -Series.			
<i>p</i> -Series.						
Compound.	$\lambda_{\text{max.}}$ $m\mu$.	$\epsilon_{\text{max.}}$ $\times 10^{-3}$.	Compound.	$\lambda_{\text{max.}}$ $m\mu$.	$\epsilon_{\text{max.}}$ $\times 10^{-3}$.	$\frac{\epsilon_{\text{max.}} \times 10^{-3}}{\text{No. of benzene nuclei}}$
Diphenyl	251.5	18.3	(Diphenyl)	251.5	18.3	9
Terphenyl ...	280	25	Terphenyl	251.5	44	14.7
Quaterphenyl	300	39	Noviphenyl	253	184	20.5
Quinquephenyl	310	62.5	Deciphenyl	253	213	21.3
Sexiphenyl ...	317.5	56	Quinquephenyl ...	254	309	20.6
(Stilbene	295	23.4)	(Tetraphenylmethane)	262	2.0	0.5

The marked difference between tetraphenylmethane and the m -series indicates for the latter a "semidiphenyl" chromophore (λ 253 $m\mu$, ϵ 20,000) functioning additively. In the p -series $\lambda_{\text{max.}}$ is converging to a limit as n increases, so that the plot of λ^2 against n would not be a straight line.⁶⁹ This can only mean that k (the restoring force) increases with nm , and for the higher members the ordinary Kekulé resonance becomes more important than in the lower members, which behave more like the conjugated polyenes.

The conjugation effect requires a planar structure for the "mobile" electrons to play their full part. The steric effects of substituents are very marked, thus bismesityl,⁷⁴ $(\text{C}_6\text{H}_2\text{Me}_3)_2$, shows $\lambda_{\text{max.}}$ 265 $m\mu$, $\epsilon_{\text{max.}}$ 560, i.e., the mesitylene spectrum doubled ($\epsilon_{\text{max.}}$ 280). Steric effects are also shown on p . 18: 75-77

⁷⁰ R. Kuhn, *Angew. Chem.*, 1937, **50**, 703.

⁷¹ W. R. Brode and J. D. Piper, *J. Amer. Chem. Soc.*, 1935, **57**, 135.

⁷² A. E. Gillam and D. H. Hey, *J.*, 1939, 1170.


⁷³ A. E. Gillam, D. H. Hey, and A. Lambert, *J.*, 1941, 364 (on phenylpyridines and pyridyldiphenyls).

⁷⁴ L. W. Pickett, G. F. Walter, and H. France, *J. Amer. Chem. Soc.*, 1936, **58**, 2296.

⁷⁵ H. Ley and H. Dirking, *Ber.*, 1934, **67**, 1331.

⁷⁶ A. Smakula and A. Wassermann, *Z. physikal. Chem.*, 1931, *A*, **155**, 353.

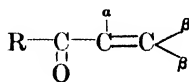
⁷⁷ H. Ley and F. Rinke, *Ber.*, 1923, **56**, 771.

		$\lambda_{\max.}, m\mu.$	$\epsilon_{\max.} \times 10^{-3}.$	$\lambda_{\max.}, m\mu.$	$\epsilon_{\max.} \times 10^{-3}.$
Ph·CH:CHPh	$\left\{ \begin{array}{l} \text{cis} \\ \text{trans} \end{array} \right.$	$\left\{ \begin{array}{l} 278 \\ 294 \end{array} \right.$	$\left\{ \begin{array}{l} 9.35 \\ 23.4 \end{array} \right.$	$\left\{ \begin{array}{l} 222 \\ 225 \end{array} \right.$	$\left\{ \begin{array}{l} 23 \\ 15.6 \end{array} \right.$
Ph·CMe:CHPh	$\left\{ \begin{array}{l} \text{trans} \\ \text{trans} \end{array} \right.$	$\left\{ \begin{array}{l} 272 \\ 241 \end{array} \right.$	$\left\{ \begin{array}{l} 18.2 \\ 11.7 \end{array} \right.$		
Ph·CMe:CMPh	$\left\{ \begin{array}{l} \text{trans} \\ \text{trans} \end{array} \right.$	$\left\{ \begin{array}{l} 262 \\ 274 \end{array} \right.$	$\left\{ \begin{array}{l} 9.1 \\ 20.8 \end{array} \right.$		
Ph·CH:CH·CO ₂ H	$\left\{ \begin{array}{l} \text{cis} \\ \text{trans} \end{array} \right.$	$\left\{ \begin{array}{l} 262 \\ 274 \end{array} \right.$	$\left\{ \begin{array}{l} 9.1 \\ 20.8 \end{array} \right.$		
Ph·N:NPh ⁷⁸	$\left\{ \begin{array}{l} \text{cis} \\ \text{trans} \end{array} \right.$	$\left\{ \begin{array}{l} 324 \\ 319 \end{array} \right.$	$\left\{ \begin{array}{l} 15.1 \\ 19.5 \end{array} \right.$	$\left\{ \begin{array}{l} 438 \\ 445 \end{array} \right.$	$\left\{ \begin{array}{l} 1.15 \\ 0.29 \end{array} \right.$
 ·N:NPh	$\left\{ \begin{array}{l} \text{cis} \\ \text{trans} \end{array} \right.$	$\left\{ \begin{array}{l} 299 \\ 322 \end{array} \right.$	$\left\{ \begin{array}{l} 8.5 \\ 20 \end{array} \right.$	$\left\{ \begin{array}{l} 447 \\ 446 \end{array} \right.$	$\left\{ \begin{array}{l} 2.2 \\ 6.8 \end{array} \right.$

A break in conjugation by insertion of $[\text{CH}_2]_n$ ($n = 1, 2 \dots$) produces a clear-cut insulating effect and the two separated chromophores function independently.

This effect is well known,⁷⁹ but the superposition of chromophores is often a more complicated affair, which is not easy to disentangle. A single isolated absorption curve drawn on a frequency scale should be symmetrical, and the band-strength $\int \epsilon \cdot d\nu$ and half-width H should be significant quantities. Variants (*e.g.*, substituents in benzene rings) giving rise to large or small inner field effects may be strongly or weakly *variochromic*, and it is convenient to describe displacement on the wave-length scale as *chromolatory*.⁸⁰ The curve for *p*-methoxystilbene is practically that of stilbene plus that of anisole, *p*-nitrostilbene is a summation of the stilbene curve slightly displaced and that of nitrobenzene, whilst *p*-nitro-*p'*-hydroxystilbene is a summation of phenol, nitrobenzene, and stilbene (displaced) absorptions. The absorption spectra of rottlerin⁸¹ and its derivatives afford a good example of both CH_2 insulation and superposition of chromophoric effects due to parts of large molecules functioning independently.

The spectra of $\alpha\beta$ -unsaturated ketones^{82, 83} show the additive and the constitutive effect clearly. The ethenoid absorption, $\text{R} \cdot \text{CO} \cdot \underset{\text{R}}{\overset{*}{\text{C}}} \cdot \text{CR}_2$ (* denoting the site of the transition), is displaced by induction from $<200 m\mu$ ($\log \epsilon_{\max.} \text{ ca. } 4$) to an extent depending on the degree of substitution :



	Substitution.	$\lambda_{\max.}, m\mu.$	No. of examples.
Mono-	α or β	225 ± 5	6
Di-	$\alpha\beta$ or $\beta\beta$	239 ± 5	36
Tri-	$\alpha\beta\beta$	254 ± 5	9
	($\beta\beta = \text{H}, \text{H}$)	218)	

⁷⁸ A. H. Cook, D. G. Jones, and J. B. Polya, *J.*, 1939, 1315.

⁷⁹ (Mme.) Ramart-Lucas, *Bull. Soc. chim.*, 1932, **51**, 289; also Grignard's "Traité de Chimie Organique," Vol. II, Paris, 1936.

⁸⁰ E. Hertel and H. Lührmann, *Z. physikal. Chem.*, 1939, *B*, **44**, 261.

⁸¹ R. A. Morton and Z. Sawires, *J.*, 1940, 1052.

⁸² R. B. Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123.

⁸³ L. K. Evans and A. E. Gillam, *J.*, 1941, 815.

The above table is of great diagnostic value. The low-intensity $\text{R} \begin{array}{c} \text{R} \\ \diagup \\ \text{C}=\text{O}^* \end{array}$ ketone band at 275 μ in acetone is displaced to 305—325 μ in (II), $\epsilon_{\text{max.}}$ remaining low (20—80 as a rule).⁸³ The acetone absorption at 187—195 μ also appears in methyl chloride, and is not displaced to 225—250 μ .^{84, 85} The effects in aromatic ketones, keto-enols, hydroxy-aldehydes, and hydroxy-ketones^{86, 87} are more complicated, but additive and constitutive effects are easily sorted out.

The effects of substitution in benzene derivatives are complicated (rather than difficult) and cannot be dealt with in detail.⁸⁸⁻⁹² It is perhaps preferable to deal fairly fully with an illustrative series and refer the reader to work on others. Simple mixtures may form loose complexes breaking down on dilution, *e.g.*, $\text{C}_6\text{H}_5\cdot\text{NO}_2 \dots \text{H}_2\text{N}\cdot\text{C}_6\text{H}_5$. In the *o*-, *m*-, and *p*-nitroanilines intramolecular forces displace absorption towards the visible, but a competing environment (containing, *e.g.*, hydrochloric or perchloric acid) reverses the process.^{93, 94} The actual absorption is additive to the extent that a transition localised in $-\text{NO}_2$ (cf. p. 11), and made more probable by induction, is superimposed upon a benzenoid transition already familiar in aniline and other derivatives of benzene. In 10% hydrochloric acid the nitroanilines exhibit merely the absorption of nitrobenzene. The concentration of perchloric acid needed to achieve this result varies :

		HClO ₄ concentration, N. ⁹³			
<i>o</i> -Nitroaniline		6		
<i>m</i> -		0.1		
<i>p</i> -		3		
Compound.		$\lambda_{\text{max.}}$, μ .	$\epsilon_{\text{max.}}$	$\lambda_{\text{max.}}$, μ .	$\epsilon_{\text{max.}}$
$\text{C}_6\text{H}_4 \begin{array}{c} \text{CH}_3 \\ \text{NH}_2 \end{array}$	<i>o</i> -	284.3	2,130	233.1	11,500
	<i>m</i> -	287.2	1,950	236.9	11,500
	<i>p</i> -	290.5	2,000	235.7	10,300
$\text{C}_6\text{H}_4 \begin{array}{c} \text{NO}_2 \\ \text{NH}_2 \end{array}$	<i>o</i> -	403.6	5,400	275.2	5,100
	<i>m</i> -	375	1,580	233	18,000
	<i>p</i> -	374	15,350	230	13,900
Nitrotoluidines.					
No. of isomers. $\text{NH}_2 : \text{NO}_2$.					
(4)	<i>o</i> -	404—417	5,000	284	5,000
				232	20,000
				(287)	4,500
(4)	<i>m</i> -	375 (352)	1,500	235	1,500
(2)	<i>p</i> -	374—379	15,000	233	7,000

⁸⁴ L. K. Wolf and W. Herold, *Z. physikal. Chem.*, 1929, **B**, **5**, 124; 1931, **B**, **12**, 165; 1932, **B**, **18**, 265.

⁸⁵ G. Scheibe and C. F. Lindstrom, *ibid.*, 1931, **B**, **12**, 387.

⁸⁶ R. A. Morton, A. Hassan, and T. C. Calloway, *J.*, 1934, 883.

⁸⁷ R. A. Morton and A. L. Stubbs, *J.*, 1940, 1347.

⁸⁸ M. Pestemer, *Angew. Chem.*, 1937, **50**, 343.

⁸⁹ K. L. Wolf and W. Herold, *Z. physikal. Chem.*, 1931, **B**, **13**, 201.

⁹⁰ K. L. Wolf and O. Strasser, *ibid.*, 1933, **B**, **21**, 389.

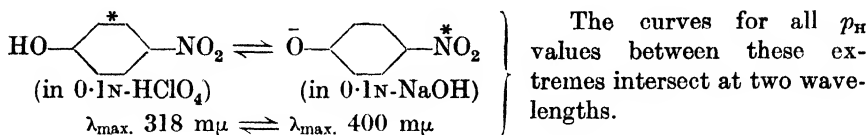
⁹¹ G. Scheibe, *Ber.*, 1926, **59**, 2618.

⁹² H. Conrad-Billroth, *Z. physikal. Chem.*, 1932, **B**, **19**, 76; 1933, **B**, **20**, 222, 227; 1933, **B**, **23**, 139; 1935, **B**, **29**, 170; 1936, **B**, **33**, 133, 311.

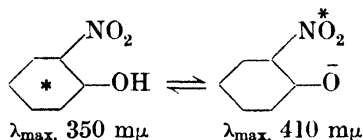
⁹³ L. Dede and A. Rosenberg, *Ber.*, 1934, **67**, 147.

With two exceptions ($\text{CH}_3:\text{NO}_2:\text{NH}_2 = 1:3:2$ and $1:4:3$) the curves in hydrochloric acid for the nitrotoluidines agree almost exactly with those of the parent nitrotoluenes.⁹⁴

The same "nitro" band reappears in *o*- and *p*-nitrophenol:⁹³

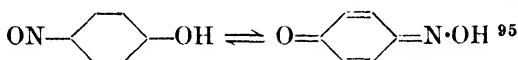


and



* Denotes the site of the electronic process.

Another example of equilibrium is afforded by *p*-nitrosophenol:

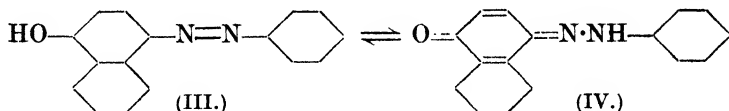


"Nitrosophenol" in ether.

	$\lambda_{\text{max.}}, \text{m}\mu.$	$\epsilon_{\text{max.}}$		$\lambda_{\text{max.}}$	$\epsilon_{\text{max.}}$
$\text{NO}-\text{C}_6\text{H}_4-\text{O}\cdot\text{CH}_3$	$\left\{ \begin{array}{l} 444 \\ 322.6 \\ 284 \end{array} \right.$	$\left\{ \begin{array}{l} 0.6 \\ 20,900 \\ 4,467 \end{array} \right.$	$\text{NO}-\text{C}_6\text{H}_4-\text{OH}$	$\left\{ \begin{array}{l} 526.3 \\ 454.5 \\ 423.7 \end{array} \right.$	$\left\{ \begin{array}{l} 1.4 \\ 8.7 \\ - \end{array} \right.$
$\text{O}=\text{C}_6\text{H}_4=\text{N}\cdot\text{O}\cdot\text{CH}_3$	$\left\{ \begin{array}{l} 436.7 \\ 416.7 \\ 392.2 \\ 294.1 \end{array} \right.$	$\left\{ \begin{array}{l} 13.2 \\ 16.22 \\ 21.4 \\ 25,120 \end{array} \right.$	$\text{O}=\text{C}_6\text{H}_4=\text{N}\cdot\text{OH}$	$\left\{ \begin{array}{l} 392.2 \\ 284 \end{array} \right.$	$\left\{ \begin{array}{l} 14.8 \\ 14,800 \end{array} \right.$

The parent substance appears to consist of 70% quinonemonoxime and 30% nitrosophenol when at equilibrium in ether.

The equilibrium (III) \rightleftharpoons (IV) affords an even clearer example of



desmotropy,⁹⁶ since in pyridine the azo-form predominates ($\lambda_{\text{max.}} 415 \text{ m}\mu$) whereas the hydrazone ($\lambda_{\text{max.}} 480 \text{ m}\mu$) preponderates in glacial acetic acid or nitrobenzene. The two forms occur in approximately equal proportion in benzene. Confirmation of this interpretation comes from the spectra of the two methyl derivatives of fixed constitution. The *o*-hydroxyazo-analogues exist almost entirely as quinonehydrazones.⁹⁷

The spectra of at least some series of benzene substitution products show

⁹⁴ R. A. Morton and A. McGookin, *J.*, 1934, 901.

⁹⁵ L. C. Anderson and M. B. Geiger, *J. Amer. Chem. Soc.*, 1932, 54, 3064.

⁹⁶ R. Kuhn and F. Bär, *Annalen*, 1935, 516, 143; see also H. Shingu, *Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1939, 35, 78.

⁹⁷ A. Burawoy, *J. pr. Chem.*, 1932, 135, 145; *J.*, 1937, 1865; 1939, 1177.

that the electronic transition located in the benzene ring may be changed (as a result of inductive effects) in discrete steps differing by a well-known vibration frequency ($\Delta\bar{\nu}$ 1450 cm.⁻¹).⁸⁷ The effect of "partial" or simple chromophoric effects functioning additively is shown clearly in anthraquinone (in alcohol) :⁹⁸

λ_{\max} , m μ	405	325.5	272.0	262.8	252.5	243.5
$\log \epsilon_{\max}$	1.95	3.75	4.31	4.31	4.71	4.52
	(b)	(a)	(b)	(b)	(a)	(a)

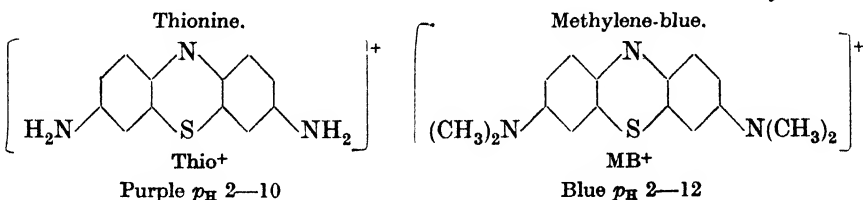
The (a) bands are due to $\text{C}_6\text{H}_4\text{CO}$ (e.g., *o*-hydroxyacetophenone) and the

(b) bands to $\text{O} \begin{array}{c} \text{R} \text{ R} \\ \diagup \quad \diagdown \\ \text{C}_6\text{H}_2 \\ \diagdown \quad \diagup \\ \text{R} \text{ R} \end{array} \text{O}$ (e.g., α -tocopherylquinone).

Heterocyclic compounds of the type of pyridine and quinoline⁹⁹ exhibit a marked resemblance to benzene and naphthalene. From the standpoint of resonance this is not surprising, and a striking similarity between the curves of acridine and anthracene has been recorded,¹ together with significant results on acridinium and phenazinium ions.

The absorption spectra of dyes in relation to resonance have been discussed for triphenylmethyl derivatives (crystal-violet, etc.).^{59, 60} A few aspects of the wider problem will be reviewed.

(a) *Polymerisation in solution.*² The two ionised dyes shown below do not follow Beer's law.



In both cases two resonating structures are postulated each with one or other of the two benzene rings in the *p*-quinonoid state :

<i>M</i> -Band	λ_{\max} , 597 m μ (Thio ⁺)	656.5 m μ (MB ⁺)
	(prominent in very dilute solutions)	
<i>D</i> -Band	λ_{\max} , 557 m μ	600 m μ
	(more prominent in concentrated solutions)	

The deviations from Beer's law are not due to formation of undissociated molecules (e.g., thionine chloride) or to ion-pairs (Thio⁺ . . Cl⁻). The *M* bands are due to monomeric and the *D* bands to dimeric ions $2\text{T}^+ \rightleftharpoons \text{T}_2^{++}$;

⁹⁸ R. A. Morton and W. T. Earlam, *J.*, 1941, 159.

⁹⁹ R. A. Morton and A. J. A. de Gouveia, *J.*, 1934, 927; D. Rădulescu and G. Ostrogoich, *Ber.*, 1931, 64, 2233.

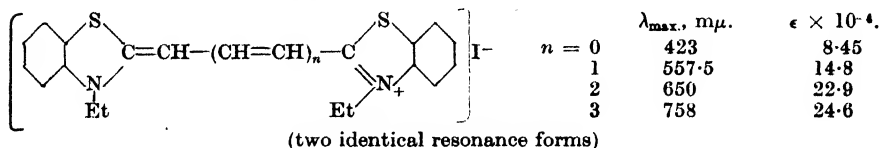
¹ *Idem*, *ibid.*

² E. Rabinowitch and L. F. Epstein, *J. Amer. Chem. Soc.*, 1941, 63, 69.

$K = [T^+]/[T_2^{++}]$; $\epsilon_{\text{obs.}} = \epsilon_M x + \frac{1}{2}\epsilon_D(1 - x)$ where ϵ_M and ϵ_D are the molecular extinction coefficients of the monomer and dimer respectively, and x is the fraction of monomer. $K = 2Cx^2/(1 - x) = 10 \times 10^4$ (thionine) or 2.8×10^4 (methylene-blue); x varies from 0.359 to 1 (thionine) or from 0.232 to 0.986 (methylene-blue). For thionine ion the temperature effect is given by $\log_{10} K = 1.9886 - 1492/T$ and the following results are obtained: free energy of dimerisation $\Delta F = -RT \ln K$ (4.9 kg.-cals./mol. at 26.7°); heat of dimerisation $\Delta H = RT^2 (d \ln K/dT)$ (6.82 kg.-cals./mol.); entropy of dimerisation $\Delta S = (\Delta H - \Delta F)/T$ (9.1 cal./mol.-degree). In pure alcohol, thionine conforms with Beer's law and the band ($\lambda_{\text{max.}}$, 603 $m\mu$) is narrower; addition of water causes the ϵ value to fall rapidly, and this corresponds with a sharp drop in the free energy of dimerisation.

Thionine fluoresces with a red light and the yield is constant for alcoholic solutions, but decreases in aqueous solution with increasing concentration (self-quenching due to the dimer). Fluorescence does not occur if the dye molecules are dimeric at the moment of excitation or if they form a dimer during the excitation period. This phenomenon is important because nearly all water-soluble dyes show D bands 1–50 $m\mu$ on the violet side of the M bands. They often form trimers and polymers, but leuco-dyes are usually monomeric. The tendency to form polymers more readily in aqueous than in alcoholic solution is at first sight strange (cf. carboxylic acids, which are dimeric in the vapour state and dissociated in water) but is explained by additive forces of the van der Waals type. The ϵ values are high, the excitation probability being often >0.5 .

The absorption spectra in the visible region of cyanine and related dyes^{5b, 3-6} afford numerous examples of intense bands in "linear oscillators" conforming to the relation $\lambda_{\text{max.}}^2 = k'n$ (p. 17) where n represents the number of $-\text{CH}=\text{CH}-$ groups, e.g.,



G. Scheibe⁶ was the first to demonstrate that reversible polymerisation is responsible for new bands in dyes. Using pinacyanol chloride, $\lambda_{\text{max.}}$ 600 $m\mu$ belongs to the monomeric ion, but if the concentration is increased or the temperature decreased a maximum at 548 due to the dimeric ion appears. Both maxima almost disappear at higher concentrations and are replaced by a third maximum at 510 $m\mu$ due to the polymeric ions.

With pseudoisocyanine (V), Scheibe has obtained results of great

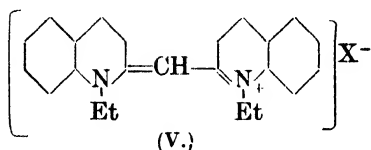
³ (Miss) N. I. Fisher and (Miss) F. M. Hamer, *Proc. Roy. Soc.*, 1936, A, **154**, 703.

⁴ W. König, *Z. wiss. Phot.*, 1935, **34**, 15.

⁵ L. G. S. Brooker, R. H. Sprague, C. P. Smyth, and G. L. Lewis, *J. Amer. Chem. Soc.*, 1940, **62**, 1116.

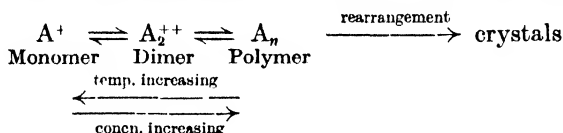
⁶ *Kolloid-Z.*, 1938, **82**, 1.

interest.^{7, 8} In alcohol the dye ion is largely monomeric (λ_{\max} . 523 m μ , ϵ_{\max} .



75,000) at 0.01M, whereas in aqueous solution the dimeric ion (λ_{\max} . 485 m μ) is already present at 0.0001M, and at concentrations >0.007M a very narrow (H 140 cm.⁻¹) intense band (λ_{\max} . 572 m μ) appears and grows more intense with

increasing concentration. The concentrated solutions are powerfully fluorescent, the fluorescence band coinciding in position and half-width with the absorption band. The appearance of the 572 m μ maximum is accompanied by a marked increase in viscosity, and the curves for viscosity-temperature, absorption-temperature, and conductivity-concentration show sharp discontinuities. For instance, when $c = 0.0144\text{M}$ the 572 m μ absorption is strong at 42° and has nearly gone at 44°. The mechanism



is not a sufficient explanation. The minimal concentration for polymer formation is lower if the dye is adsorbed on a surface (e.g., 0.0003M on freshly cleaved mica), and the polymer maximum at 572 m μ appears accompanied by a further band at 579 m μ . Adsorption depends on the structure of the

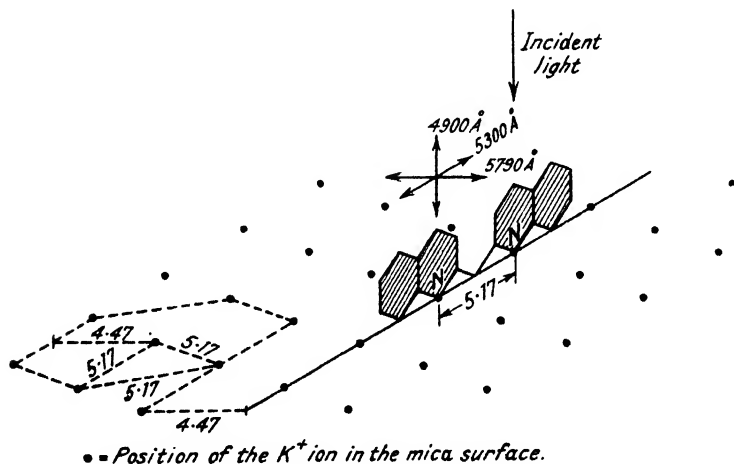


FIG. 1.

solid (calcium fluoride is here useless) and the crystal structure of mica presents K ions suitably disposed for the reception of planar pseudoisocyanine ions as shown in Fig. 1 (adapted from Scheibe's figure). If a mixed crystal of quinaldine ethiodide and pseudoisocyanine iodide is obtained (from alcohol) the dye ions will be parallel, and it is found that the character-

⁷ E. E. Jelley, *Nature*, 1937, **139**, 631.

⁸ G. Scheibe, *Angew. Chem.*, 1939, **52**, 631.

istic absorption in polarised light occurs only when the electric vector of the light is parallel to the plane of the molecules (λ_{\max} , 545, 490 $m\mu$), whereas vertically to the plane only weak and modified absorption (λ_{\max} , 530 $m\mu$) occurs. The monomeric ion gives rise to two electronic transitions, *ca.* 530 $m\mu$ in the direction of the long x axis of the planar molecule, and *ca.* 490 $m\mu$ in that of the y axis. In the dimeric ion this second band is intensified, and in the polymer the 573 $m\mu$ absorption arises in the z axis because a giant molecule is formed (rather like a stack of coins) to form a cylinder or filament (Fig. 2; after Scheibe).

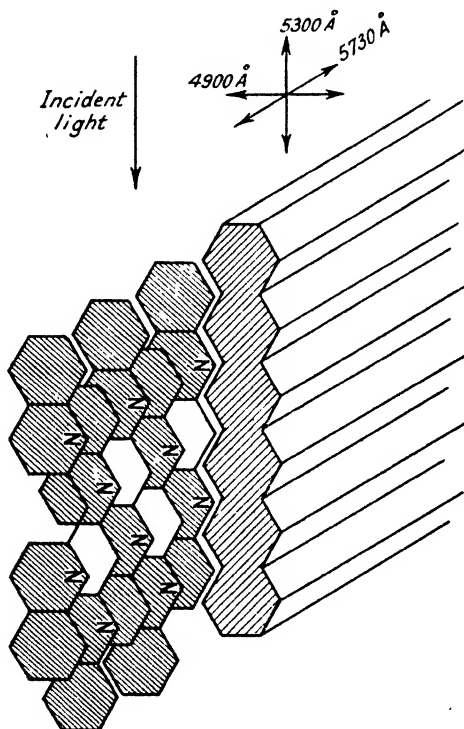
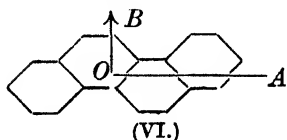


FIG. 2.

Polymerisation in aqueous solution.

The directional effect has also been shown for chrysene single crystals.⁹ The crystal structure is known.¹⁰ The unit cell [see (VI)] contains 4 molecules,



two oriented so that their OA directions make with the a and b axes angles of 102° and 90.5° respectively, and the OB directions angles of 118.4° and 29° . The orientations of the other two molecules are obtained by reflection from the (010) plane. The crystal is used in the form

⁹ K. A. Krishnan and P. K. Seshan, *Proc. Indian Acad. Sci.*, 1938, 487.

¹⁰ J. Iball, *Proc. Roy. Soc.*, 1934, A, 146, 140.

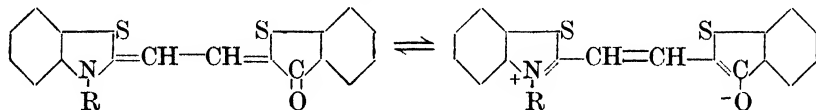
of a flake parallel to the $c(001)$ plane, and the molecular planes make angles of $\pm 29.5^\circ$ with the b axis. The absorptions in different directions at $397 \text{ m}\mu$ (first maximum) differ in intensity exactly as would be expected :

$$k_a/k_b = 310/1020 = \tan^2 29^\circ$$

and the ratio of fluorescence intensities ($420, 438, 449 \text{ m}\mu$ excited by $365 \text{ m}\mu$ Hg) is $a/b = 0.4$, corresponding to 32° . In addition to these neat results, it is clear that the light vibrations incident along the normal to the molecular plane are not absorbed at all.

The study of optical sensitising of silver halides in relation to the absorption spectra and constitution of dyes has recently advanced considerably.¹¹ The sensitising spectrum is usually closely related to the absorption spectrum of the dissolved dye, but λ_{max} (sensitising) is $> \lambda_{\text{max}}$ (ethyl-alcoholic solution) by at least $15 \text{ m}\mu$.¹² The absorption spectra of dyed silver halides (*i.e.*, of adsorbed dyes) have been measured and found to coincide with the sensitising spectra,^{13, 14} so that the distribution of spectral sensitivity (in the visible) is equivalent to the *adsorption spectrum*.

In order to give precision to the concept of *adsorption energy*, certain non-ionising dyes have been studied in the vapour state. One of these, a merocyanine,¹¹ shows at $250^\circ \lambda_{\text{max}}$ $470 \text{ m}\mu$ (with subsidiary bands at 505 ,



445 and $420 \text{ m}\mu$). The band system is displaced as a whole in solutions ($\Delta \text{ cm}^{-1}$ remaining ~ 1000). The structure recalls that of the polyenes :¹⁵

$$\nu = \bar{\nu}_0 + l\bar{\nu}' + m\bar{\nu}'', \text{ where } \bar{\nu}' = 1590 \text{ cm}^{-1} \text{ and } \bar{\nu}'' = 1240 \text{ cm}^{-1} \\ (l \text{ and } m = 0, 1, 2, 3, \text{ etc.})$$

The absorption of the merocyanine in the visible arises then from an electronic transition on which are superimposed $-\text{CH}=\text{CH}-$ vibrational quanta, etc. In aromatic hydrocarbons there is progressive relaxation of the $-\text{CH}=\text{CH}-$ link :

Ph·[CH:CH] _n ·Ph.	Anthracene.	Naphthalene.	Benzene.
1600	1430	1360	900 cm^{-1}

The greater complication of the cyanine dyes results in the superposition of a variety of vibrational frequencies, but the predominance of $-\text{CH:CH}-$ is often quite clear. In itself this fact affords no more than a clue, for the values of λ_{max} and ϵ_{max} are much more sensitive to structural changes than would be expected from simple analogies. The location of the long-wave

¹¹ S. E. Sheppard, R. H. Lambert, and R. D. Walker, *J. Chem. Physics*, 1941, **9**, 96.

¹² *E.g.*, (Miss) F. M. Hamer, *Phot. J.*, 1922, **62**, 8; O. Bloch and (Miss) F. M. Hamer, *ibid.*, 1928, **68**, 22; L. G. S. Brooker, G. H. Keyes, and F. L. White, *J. Amer. Chem. Soc.*, 1935, **57**, 2492.

¹³ S. Natanson, *Nature*, 1937, **140**, 197 (erythrosin and phloxine).

¹⁴ J. A. Leermakers, B. H. Carroll, and C. J. Stand, *J. Chem. Physics*, 1937, **5**, 875.

¹⁵ K. W. Hausser, *Z. tech. Physik*, 1934, **15**, 10.

maximum in a cyanine dye depends upon the shape of the molecule [the most extended form of the molecule (Mulliken); the greatest range in the molecule of electron transfer (Pauling)]. The electrons make the transit by moving from atom to atom, and this "appears to be consonant with the superposition of a vibrational frequency possible to a given link." The spectrum may also be decisively modified by the character of the nuclei (quinoline, thiazole, etc.) even in the visible region.* Dominating everything else, however, is the possibility of a planar configuration for the dye molecule. This allows the fullest development of resonance, and of a transition polarised in the plane of the molecule. Even with planar structures, different stereoisomers will differ with regard to the extent to which they undergo edge-on adsorption to silver halide. On this basis coplanar coupling of electronic displacements in the dye and in a congruent plane of the silver halide lattice is a key factor in the whole problem of sensitising. In some cyanine dyes the ϵ values of planar isomers are twice those of non-planar isomers, and the former alone are effective sensitisers. Electrons of the Br^- ions have a vector E_a in the 111 plane, and this component may undergo coupling with a parallel component of the resonance energy of the adsorbed dye. This would correspond to the adsorption energy and to the displacement of λ_{max} . (adsorbed dye \longrightarrow vapour), and implies that the coupling proceeds prior to adsorption and hence in the ground levels. The progress of this work will be followed with interest.

Attention is also drawn to the following publications :

(a) *Review articles.*

Photoelectric Spectrophotometry : G. Kortum (*Angew. Chem.*, 1937, **50**, 193).

Colorimetric, Spectrophotometric and Spectrographic Methods : G. Kortum and M. Seiler (*Angew. Chem.*, 1939, **52**, 687).

Spectrometric Studies in Relation to Biology : T. R. Hogness and V. R. Potter (*Ann. Rev. Biochem.*, 1941, **10**, 509).

Practical Aspects of Absorption Spectrophotometry : R. A. Morton (Institute of Chemistry, 1938).

(b) *Books.*

Absorption Spectrophotometry and its Applications : Bibliography and Abstracts, 1932—1938 (866 papers) : O. J. Walker (Adam Hilger, London, 1939).

Absorption Spectra of Natural Products : F. Ellinger, *Tabulæ Biologicæ*, Vol. XII (W. Junk, Den Haag, 1937).

Lösungsspektren : H. Mohler (G. Fischer, Jena).

Chemical Spectroscopy : W. R. Bröde (John Wiley and Sons, and Chapman and Hall, 1939).

* Cf. Morton and Stubbs, *loc. cit.*, ref. (87). This effect is to be distinguished from the superimposed ultra-violet absorption of *parts* of the large molecule.

The Identification of Molecular Spectra: R. W. B. Pearse and A. G. Gaydon (Chapman and Hall, London, 1941).

Absorption Spectra of Vitamins, Hormones, and Co-enzymes: R. A. Morton (Adam Hilger, London, Second edn., 1942), also *Ann. Rev. Biochem.*, 1942, **12**, article on Fat-soluble Vitamins.

Proceedings of Conferences on Spectroscopy held annually at the Massachusetts Institute of Technology, Vols. I—VI, Ed. G. R. Harrison (John Wiley, New York).

Molekülspektren von Lösungen und Flüssigkeiten: G. Scheibe and W. Frömel (Eucken-Wolf, Hand- und Jahrbuch der chemischen Physik, Band 9, Abschnitt III—IV, 142, 1937).
R. A. M.

3. DIAMAGNETISM.

Recent Annual Reports do not contain many references to magnetochemistry. In the last volume the application of magnetochemistry to free radicals was discussed,¹ and in 1937 H. Terrey and O. J. Walker² reviewed its application to the rare-earth elements. No summary of work on diamagnetism has been given for at least 10 years, and it is the aim of this Report to summarise the present state of knowledge in this branch of magnetochemistry, to review the applications of diamagnetic-susceptibility measurements to problems of molecular structure, and to indicate several interesting and promising new lines of application which were being studied just before the outbreak of war.

The fundamental investigations in diamagnetism are associated with the names of Curie, Pascal, and Langevin. On the experimental side, the extensive and systematic investigations of P. Pascal³ on organic compounds showed that the diamagnetic susceptibility of a molecule, χ_M ($\chi_M = \chi \cdot M$, where χ is the mass susceptibility and M is the molecular weight), is an additive and constitutive property. Hence, for a compound $X_aY_bZ_c$, $\chi_M = a\chi_X + b\chi_Y + c\chi_Z + \lambda$, where a , b , and c are the numbers of atoms of X, Y, and Z having, respectively, susceptibilities χ_X , χ_Y , and χ_Z , and λ is a constitutive correction constant dependent upon the nature of the chemical linkings between the different atoms. From classical theory, P. Langevin⁴ derived mathematical expressions for the susceptibilities of atoms which show that diamagnetism is independent of temperature. Since these investigations, a considerable amount of work has been done on both the experimental and the theoretical side. In the main, this Report will deal with experimental aspects of more recent work.

An excellent general review of magnetochemistry was given by (Sir)

¹ D. H. Hey, *Ann. Reports*, 1940, **37**, 263.

² *Ibid.*, 1937, **34**, 126.

³ *Ann. Chim.*, 1909, **16**, 531; 1910, **19**, 5; *Bull. Soc. chim.*, 1911, **9**, 79, 177, 336, 809, 868.

⁴ *Ann. Chim. Phys.* 1905, **5**, 70.

S. S. Bhatnagar⁵ in 1938 and general advances are discussed in several recent monographs.⁶

There is still considerable confusion in the literature owing to the divergence in the recorded values of χ for many compounds. This may arise from the fact that χ may be measured by a variety of methods and it is questionable if all these are of equal accuracy. Although none of the methods involves a highly-skilled technique, each possesses inherent errors and it would help greatly in assessing recorded values if more details of experimental procedure were given when data are published, *e.g.*, number of determinations made, methods of calibrating apparatus, reference substances, methods of purification, criteria of purity, and temperature.

(1) *The Susceptibility of Water*.—It is usual to calibrate apparatus by measuring the susceptibility of some compound for which the value of χ is well established, and H. R. Nettleton and S. Sugden⁷ have discussed this problem in detail in their investigation of the susceptibility of nickel chloride. Following P. Pascal,⁸ many investigators use water as reference substance. [Pascal records χ of water as -0.75 * but, since the value accepted today is -0.720 , all his recorded values must be corrected by multiplying them by $0.72/0.75 = 0.96$.] The employment of water as reference substance requires that the water must be subjected to a rigorous purification process, otherwise all data will be vitiated. To obtain water of $\chi = -0.72$ is much more difficult than many investigators appear to believe. A. P. Wills⁸ showed that χ_{18° was -0.72 and remained practically constant at different field strengths; P. Sève⁹ found -0.72 , W. J. de Haas and P. Drapier¹⁰ recorded -0.721 , and A. Piccard and A. Devaud^{10a} give χ_{20° as -0.71864 , slightly less than -0.72183 , the value found by H. Auer.¹¹ Several investigators have measured χ for water at different temperatures and, generally, they found that the value increases with rising temperature. For instance, R. N. Mathur¹² found that χ increased from -0.7195 at 15° to -0.7297 at 75° , M. A. Azim, S. S. Bhatnagar, and R. N. Mathur¹³ report an increase from -0.720 at 25° to -0.726 at 75° , and H. Auer,¹¹ in a very accurate determination, gives $\chi_{16.3^\circ}$ as -0.72145 ± 0.00048 and χ_{20° as -0.721834 ± 0.00048 . P. S. Varadachari,¹⁴ on the other hand,

⁵ *Proc. Twenty-fifth Indian Sci. Congress*, 1938, II, 49; summarised in *Science and Culture*, 1938, 3, 446.

⁶ E. C. Stoner, "Magnetism and Matter," Macmillan, London, 1934; L. F. Bates, "Modern Magnetism," Cambridge, 1939; B. Cabrera, "Dia- et Paramagnétisme et Structure de la Matière," Hermann, Paris, 1937; S. S. Bhatnagar and K. N. Mathur, "Physical Principles and Applications of Magnetochemistry," Macmillan, London, 1935; W. Klemm, "Magnetochemie," Akademische Verlagsgesellschaft M.B.H., Leipzig, 1936; J. H. van Vleck, "Theory of Electric and Magnetic Susceptibilities," Oxford, 1932.

⁷ *Proc. Roy. Soc.*, 1939, A, 173, 313.

⁸ *J. Physique*, 1913, 3, 8.

^{10a} *Arch. Sci. phys. nat.*, 1920, 2, 455.

¹² *Indian J. Physics*, 1931, 6, 207.

¹⁴ *Proc. Indian Acad. Sci.*, 1935, A, 2, 161.

⁸ *Physical Rev.*, 1905, 20, 188.

¹⁰ *Ann. Physik*, 1913, 42, 673.

¹¹ *Ann. Physik*, 1933, 18, 593.

¹³ *Phil. Mag.*, 1933, 16, 580.

* All values of χ in this Report have been multiplied by 10^6 .

found a much smaller increase (-0.7200 at 28° ; -0.7216 at 55°). W. Johner¹⁵ put forward the formula $\chi_\theta = \chi_{20}[1 + 0.00013(\theta - 20)]$ for the temperature coefficient of the susceptibility of water, and later, A. P. Wills and G. F. Boeker¹⁶ deduced a parabolic formula for the variation of χ with temperature for 14 temperatures in the range $20-66^\circ$, but this is contested by B. Cabrera and H. Fahlenbrach¹⁷ who state that water has a positive temperature coefficient and that χ increases linearly with temperature. K. Honda and Y. Shimizu¹⁸ have calculated theoretically the variation of χ with temperature.

This variation of χ with temperature appears to contravene the statement that diamagnetism is independent of temperature but it is probably due to simplification of the molecular species present in water as a result of the breakdown of hydrogen-bonded structures at the higher temperatures.¹⁹ Support is lent to this view by the fact that L. Sibaiya²⁰ records that χ for ice is constant from -120° to 0° and is -0.708 , considerably lower than the value for water. B. Cabrera and H. Fahlenbrach, however, have found that the susceptibility of ice ($\chi_0 = -0.7019$) varies linearly with temperature between -60° and 0° ,²¹ but that above 100° χ of water is constant.²²

That the presence of isotopic analogues does not affect the value of χ_M has been experimentally substantiated by P. W. Selwood and A. A. Frost,²³ (Miss) V. C. G. Trew and J. F. Spencer,²⁴ F. E. Hoare,²⁵ and V. Nehra and M. Qureshi²⁶ from measurements on deuterium oxide. F. W. Gray and J. H. Cruickshank²⁷ measured H_2O-D_2O mixtures containing 44, 62, and 87% of D_2O and concluded that H_2O , HOD , and D_2O have identical values of χ_M , whilst, from similar measurements, H. P. Iskenderian²⁸ has deduced values of -0.6807 and -0.6466 for χ of HOD and D_2O , respectively. B. Cabrera and H. Fahlenbrach have investigated the magneto-thermal behaviour of D_2O but, since they report²⁹ that its molecular susceptibility differs from that of H_2O , their statement³⁰ that, between -60° and 150° , $d\chi/d\theta$ is faster in solid and slower in liquid D_2O than in H_2O must be accepted with reserve. On the Thomas-Fermi atom model, T. Takéuchi, T. Sugita, and T. Inai³¹ have calculated the susceptibility and $d\chi/d\theta$ for D_2O .

It would, therefore, appear that the choice of water as a standard reference substance is not a particularly happy one.

(2) *Effect of Temperature on Other Diamagnetic Substances.*—Little attention has been given to this problem, and available data are not

¹⁵ *Helv. Physica Acta*, 1931, **4**, 238.

¹⁶ *Physical Rev.*, 1934, **46**, 907.

¹⁷ *Z. Physik*, 1933, **82**, 759.

¹⁸ *Sci. Rep. Tôhoku Imp. Univ.*, 1937, **25**, 939.

¹⁹ W. R. Angus and W. K. Hill, *Trans. Faraday Soc.*, 1940, **36**, 923.

²⁰ *Current Sci.*, 1935, **4**, 41.

²¹ *Anal. Fis. Quím.*, 1933, **31**, 401.

²² *Ibid.*, 1934, **32**, 525.

²³ *J. Amer. Chem. Soc.*, 1933, **55**, 4335.

²⁴ *Nature*, 1936, **137**, 998.

²⁵ *Ibid.*, p. 497.

²⁶ *Current Sci.*, 1937, **5**, 533.

²⁷ *Nature*, 1935, **135**, 268.

²⁸ *Physical Rev.*, 1937, **51**, 1092.

²⁹ *Anal. Fis. Quím.*, 1934, **32**, 538.

³⁰ *Naturwiss.*, 1934, **22**, 417.

³¹ *Bull. Tokyo Univ. Eng.*, 1937, **6**, 116.

sufficiently plentiful to permit an unequivocal explanation of observed effects. There appear to be three classes of substance: (i) a group which shows, like water, a positive temperature coefficient, but the only data are for *n*- and *iso*-propyl and -butyl alcohols;¹³ (ii) those which have a negative temperature coefficient and comprise, almost entirely, aromatic derivatives;^{12, 13, 32} and (iii) those which are independent of temperature. In the last group are hydrogen,³³ the rare gases,³³ boron³⁴ (from -183° to 20°), cyclohexane and carbon tetrachloride¹³ (20 – 75°), acetic¹⁴ (25 – 55°) and *n*- and *iso*-butyric acids,¹² butyl bromide,¹² and, unexpectedly, *iso*amyl alcohol¹² (20 – 80°). P. S. Varadachari¹⁴ has examined the system sodium sulphate–water throughout the range 25 – 55° but finds no change at 33° the temperature of transition from decahydrate to anhydrous salt. Various tentative explanations have been advanced. M. A. Azim, S. S. Bhatnagar, and R. N. Mathur¹³ have attempted to correlate their results with the polarisability and high associating tendency of substances having a positive coefficient. The non-polar, symmetrical characters of cyclohexane and carbon tetrachloride are attributed by the same authors as reasons for the temperature-independence of χ of these compounds; but this is an *ad hoc* explanation which is inapplicable to butyl bromide and the fatty acids. The negative coefficient exhibited by aromatic compounds finds no explanation, but there is the interesting observation of S. R. Rao and S. Sriraman³⁵ that χ of nitrobenzene, in the range 30 – 102° , slowly diminishes to a minimum value at 75° and then increases, a behaviour which they attribute to changes in association. More work in this direction might yield some extremely interesting results and relationships.

(3) *Influence of Physical State on the Value of χ* .—The big increase in χ_M on vaporisation reported by V. I. Vaidyanathan³⁶ for a number of organic compounds must be doubted because, more recently, R. Jaanus and J. Schur³⁷ have reported a value for benzene vapour of -59 ± 3 which is of the same order of magnitude as the accepted value of -55.0 for liquid benzene, the difference probably being due to the greater difficulty of measuring χ for gases. Likewise, the influence of fusion is not clear. B. Cabrera and H. Fahlenbrach³⁸ state that a sudden change occurs on fusion due to deformations caused by crystal forces, whereas T. Ishiwara³⁹ found no discontinuity at the melting points of silver halides. There is good reason to believe, however, that the liquid state has a slightly higher value for χ than the solid state. This is borne out by the work of A. E. Oxley⁴⁰ on organic compounds. Also, J. Farquharson and E. Heymann⁴¹ have

³² S. S. Bhatnagar, M. B. Nevgi, and M. L. Khanna, *Z. Physik*, 1934, **89**, 506; G. F. Boeker, *Physical Rev.*, 1933, **43**, 756.

³³ G. G. Havens, *Physical Rev.*, 1933, **43**, 992.

³⁴ L. Klemm, *Z. Elektrochem.*, 1939, **45**, 354.

³⁵ *Indian J. Physics*, 1934, **8**, 315.

³⁶ *Ibid.*, 1927, **2**, 135.

³⁷ *Nature*, 1934, **134**, 101.

³⁸ *Compt. rend.*, 1933, **197**, 379; *Z. Physik*, 1934, **89**, 682.

³⁹ *Sci. Rep. Tôhoku Imp. Univ.*, 1920, **9**, 233.

⁴⁰ *Phil. Trans.*, 1914, **214**, 109; 1915, **215**, 79; 1926, **220**, 247.

⁴¹ *Trans. Faraday Soc.*, 1935, **31**, 1004.

examined cadmium, mercurous, and lead chlorides as powders, solidified melts, and in the molten state. They found that χ increased in this order and, since the value of χ for an aqueous solution of cadmium chloride was found to decrease with increasing concentration of the salt, they suggested that the increase in χ on melting may be due to ionisation. Y. Shimizu⁴² has reported abrupt changes at the melting points and transition points of a number of metals, whilst G. E. R. Schulze⁴³ found a slight change at the transition points of ammonium bromide and nitrate, potassium and thallous nitrates, and silver iodide. Ammonium halides have also been examined by A. Dinsdale and F. A. Long.^{43a} The observed effects are attributed to lattice changes. K. C. Subramaniam⁴⁴ attributes the increase in χ of benzophenone on melting to breakdown of polymerides, and gives the same explanation for the diminution of χ on melting *p*-nitrotoluene. Here is another fertile field of enquiry from which much interesting information should be forthcoming.

(4) *The Diamagnetic >CH₂ Increment.*—The values (corrected) given by P. Pascal³ for the introduction of a methylene group vary from -11.86 to -11.42 . The determination of this value is fundamentally important to the determination of values for atoms in organic molecules and for bonding and constitutive correction constants because these derived values form the basis of the testing of the additivity of diamagnetism. Many workers have accepted Pascal's values, but others have pointed out discrepancies. A critical examination of Pascal's data made by (Sir) S. S. Bhatnagar and N. G. Mitra⁴⁵ led them to suggest that the (numerically) maximum value was -11.68 . B. Cabrera and H. Fahlenbrach⁴⁶ give -11.48 from measurements on seven alcohols; D. B. Woodbridge⁴⁷ obtained -11.67 from acetic acid and five alkyl acetates; F. W. Gray and J. H. Cruickshank⁴⁸ report -11.87 from an investigation of homologous organic nitrates, nitrites, and nitro-compounds; J. Farquharson and M. V. C. Sastri,⁴⁹ from five normal aliphatic acids, deduced -11.64 ; and -11.36 was obtained by (Sir) S. S. Bhatnagar, N. G. Mitra, and G. D. Tuli⁵⁰ from an examination of twenty compounds belonging to four different homologous series. This was the unsatisfactory state of affairs in 1938 when a systematic re-investigation,* under carefully controlled conditions, was started at the University College of North Wales, Bangor. About 50 compounds were measured when the work had to be discontinued, but analysis of the ascertained data

⁴² *Sci. Rep. Tôhoku Imp. Univ.*, 1937, **25**, 921.

⁴³ *Z. physikal. Chem.*, 1938, *B*, **40**, 308.

^{43a} *Proc. Leeds Phil. Soc.*, 1937, **3**, 270.

⁴⁴ *Proc. Indian Acad. Sci.*, 1936, *A*, **3**, 420.

⁴⁵ *J. Indian Chem. Soc.*, 1936, **13**, 329.

⁴⁶ *Z. Physik.* 1933, **85**, 568.

⁴⁷ *Physical Rev.*, 1935, **48**, 672.

⁴⁸ *Trans. Faraday Soc.*, 1935, **31**, 1491.

⁴⁹ *Ibid.*, 1937, **33**, 1472.

⁵⁰ *Phil. Mag.*, 1934, **18**, 449.

* Full details will be given in forthcoming papers by W. R. Angus, W. K. Hill, and E. Roberts.

on aliphatic alcohols, acids, esters, aldehydes, and ketones, and aromatic hydrocarbons and esters yields the value of -11.68 ± 0.01 . This value was obtained by the subtraction method of P. Pascal³ and by a graphical method⁴⁹ in which observed values of χ_M are plotted against the number of methylene groups. The straight line obtained can be represented by the equation $\chi_M = an - b$, where b is the intercept on the χ_M axis and represents the diamagnetic effect of the "end" group, and a is the diamagnetic increment of a methylene group, of which there are n in the molecule. By subtracting b from the observed χ_M value the contribution made by n methylene groups is obtained, and hence the $>\text{CH}_2$ increment. This method is preferable to that of Pascal in that it involves each member of the series independently, whereas his method yields a mean value for χ_{CH} , which is dependent on the purity of the first and the last member of the series only—intermediate members can be neglected. Further work on a wide variety of series will be continued when conditions permit, because, although the data are self-consistent for each series, the values of $\chi_{>\text{CH}}$, derived for the different series vary from -11.65 to -11.72 . Other interesting results obtained in this investigation are (i) that when an acid is converted into its methyl ester the increment is -10.66 , i.e., about 1 unit less than the average value of $\chi_{>\text{CH}}$; (ii) that branched methyl substitution causes the susceptibility to increase by approximately -12.70 irrespective of whether an *iso*- or a *sec*-compound is formed, i.e., about 1 unit greater than the average value of $\chi_{>\text{CH}}$; and (iii) a second branched methyl substitution gives the usual increment of -11.68 . These results amply demonstrate the necessity for fundamental investigations on homologous series before applications to problems of molecular structure can be reliably made.

(5) *Diamagnetism of Isomerides*.—From the viewpoint of Pascal's additivity rule the susceptibilities of isomeric compounds should be identical. Many recorded data confirm this, but a critical examination of available data indicates that this identity is probably fortuitous. For instance, although a number of isomeric pairs show identical values,^{50, 51} P. Pascal^{51a} records for ethyl butyl ketones the following values: *tert*-, -82.2 ; *iso*-, -81.9 ; *n*-, -81.1 . This sequence has been borne out by later workers, and a comprehensive discussion of the question by (Sir) S. S. Bhatnagar, R. N. Mathur, and M. B. Nevgi⁵² led them to conclude that, generally, the susceptibilities of isomeric compounds were: *tert*- $>$ *sec*- \sim *iso*- $>$ *n*-; $o > p > m$; *cis* $>$ *trans*. They also state that the susceptibilities of the *n*-, *iso*-, and *tert*-aliphatic isomerides fall into the above sequence as a result of change in the radii of the electronic orbits owing to changes in the effective electronic charges. Various attempts to correlate these differences with other physical data have been made⁵³ but none has proved successful. This arises partly from the paucity of data and partly from conflicting values, particularly for aromatic isomerides as is shown in the following table.

⁵¹ (a) Pascal, *Compt. rend.*, 1909, **149**, 342; (b) Bhatnagar and C. L. Dhawan, *Phil. Mag.*, 1928, **5**, 536.

⁵² *Z. Physik*, 1931, **69**, 373.

Compound.	Values of $-\chi_M \times 10^6$.			Ref.
	<i>o</i> .	<i>m</i> .	<i>p</i> .	
Cresol	73.62	73.32	72.75	53b
	73.54	72.30	71.32	54
	72.4	71.4	72.1	55
	76.94	75.70	—	53b
Nitrotoluene	71.85	72.42	70.89	54
	74.3	72.8	70.6	55
	75.65	72.97	—	53a
Toluidine	76.0	74.6	72.1	55
	101.1	—	95.9	53a
Phenetidine	102.4	—	97.4	12
	66.83	—	65.54	53b
Chlorophenol	78.3	—	76.7	55

For aliphatic isomerides the sequence given above has been found by many workers, but widely different values for the numerical increase in going from the *n*- to the *iso*-isomeride have been recorded, ranging from -0.74 to -2.74 .⁵⁶ From a recent study* of homologous series of aliphatic alcohols, acids, and esters, carried out by Mr. W. K. Hill, the following conclusions can be drawn: (i) position isomeric esters have identical susceptibilities; (ii) the susceptibility of the corresponding isomeric acid is numerically greater by approximately 1 unit; (iii) all *n*-isomeric esters have identical susceptibilities, as also have all *iso*-isomeric esters; (iv) the susceptibility of an *iso*-isomeride is greater than that of the *n*-isomeride by an approximately constant amount (-1.03); and (v) the sequence is *tert.*-slightly $>$ *sec.* \approx *iso*- $>$ *n*-.

(6) *Atomic and Ionic Susceptibilities*.—The derivation of values for the gram-atomic or gram-ionic susceptibilities from experimental data was first carried out by P. Pascal.³ He obtained susceptibilities for atoms linked together by homopolar bonds and, hence, his derived values contain bonding effects. These values enabled him to demonstrate the additive nature of diamagnetism and are probably substantially of the correct order of magnitude. When the atom participates in forming a polar salt, the molecular susceptibility of the salt may be considered as the sum of the susceptibilities of the ions, $\chi_M = \chi_{\text{cation}} + \chi_{\text{anion}}$. Values for ionic susceptibilities have been derived by two methods—from experimental data and, for spherically symmetrical ions, from theoretical calculation. The lack of agreement in experimental data published by different workers renders comparison of values derived by different methods difficult and, possibly, has led to the publication of so many methods of obtaining these values. In each method certain assumptions are made which frequently cannot be completely justified.

The divergence amongst recorded values was pointed out⁵⁷ some years

⁵³ (a) (Sir) S. S. Bhatnagar and R. N. Mathur, *Phil. Mag.*, 1931, **11**, 914; (b) (Sir) S. S. Bhatnagar, R. N. Mathur, and R. S. Mal, *ibid.*, 1930, **10**, 101.

⁵⁴ B. Cabrera and H. Fahlenbrach, *Z. Physik*, 1934, **89**, 682.

⁵⁵ K. Kido, *Sci. Rep. Tôhoku Imp. Univ.*, 1936, **24**, 701.

⁵⁶ B. Cabrera and A. Madinaveitia, *Anal. Fis. Quím.*, 1932, **30**, 528; see also Refs. 12, 13, 51a, 52, 53a, 53b.

⁵⁷ W. R. Angus, *Proc. Roy. Soc.*, 1932, **A**, 136, 569.

* A detailed discussion will be published later by W. R. Angus and W. K. Hill.
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ago in a review of the methods and is again stressed in a recent review by (Miss) V. C. G. Trew,⁵⁸ in which she summarises the various methods and obtains an average set of values for ionic susceptibilities derived from experimental results. These methods will be considered first. The wide variation in them will be self-evident, and the necessity for an early re-investigation of the whole problem will be fully apparent from an examination of the values collected in the table below. G. Joos,⁵⁹ using the data of J. Koenigsberger,⁶⁰ obtained values for salts having ions with an inert-gas configuration, *e.g.*, potassium chloride and rubidium bromide, by assuming that such ions contribute amounts to the molecular susceptibility which are inversely proportional to the square of the nuclear charge. K. Ikenmeyer⁶¹ applied this method to his measurements on alkali and alkaline-earth halides but, later, G. W. Brindley⁶² modified the method by taking the susceptibilities as inversely proportional to the squares of the effective nuclear charges evaluated by using the screening constants and effective quantum numbers proposed by J. C. Slater.⁶³ G. W. Brindley and F. E. Hoare⁶⁴ have measured the susceptibilities of crystalline alkali and alkaline-earth halides and, taking the value of $\chi_{Li} = -0.7$, which is the calculated value, they derived values for the other metallic ions and for halide ions, justifying their procedure on the grounds that, since χ_{Li} is so small, any error in it will not greatly influence the values for the other ions. They also showed that increasing co-ordination causes a slight decrease in diamagnetism, *i.e.*, gives a numerically larger value for χ_M . Thus, the change from the usual 6-co-ordination of alkali halides to 8-co-ordination in caesium iodide is accompanied by a diminution of 3.1 units.

P. Weiss⁶⁵ has employed two methods of obtaining values for ionic susceptibilities. In the first, he takes Pascal's values for atoms and adds + 3 units for a univalent anion and - 3 and - 6 units for uni- and bi-valent cations, respectively. This unwarrantable procedure neglects the specific bonding effects of different ions. In the second method, he shows that diamagnetic susceptibilities of aqueous solutions are influenced by the action of charged ions on the water molecules in the same way as molecular refraction is influenced. From the relationship $\Delta R/R = 2\Delta\chi/\chi$ he deduces that the hydrogen ion has an effective paramagnetism of + 1.1 units. The value of a halogen ion will thus be more diamagnetic by 1.1 units than the corresponding halogen acid. By this method Weiss derived values for alkali and halide ions from the measurements of R. Hocart⁶⁶ and K. Reicheneder.⁶⁷ This method has also been used by L. Abonnenc,⁶⁸

⁵⁸ *Trans. Faraday Soc.*, 1941, **37**, 476.

⁵⁹ *Z. Physik*, 1923, **19**, 347; 1925, **32**, 835.

⁶⁰ *Ann. Physik*, 1898, **66**, 698.

⁶¹ *Phil. Mag.*, 1931, **11**, 786.

⁶² *Proc. Roy. Soc.*, 1935, **A**, **152**, 342; see also F. E. Hoare and G. W. Brindley, *ibid.*, 1937, **A**, **159**, 395.

⁶³ *J. Physique*, 1930, **1**, 185.

⁶⁴ *Ann. Physik*, 1929, **3**, 58.

⁶⁵ *Ibid.*, 1929, **1**, 169.

⁶⁶ *Physical Rev.*, 1930, **36**, 57.

⁶⁷ *Compt. rend.*, 1929, **188**, 1151.

⁶⁸ *Compt. rend.*, 1934, **198**, 2237.

V. Veiel,⁶⁹ and O. E. Frivold⁷⁰ on their measurements on aqueous solutions of metallic halides. K. Kido⁷¹ has found, contrary to existing evidence, that the numerical value of χ_M for salts of metals in the same group of the periodic classification with a common anion increases linearly with the number of electrons in the cation. When χ_M is plotted against the number of electrons in the cation the intercept of the χ_M axis will give the value corresponding with the parent acid of the anion; and, by assuming that $\chi_H = 0$, he thus obtains a value for the anion. Miss Trew⁵⁸ has added another method, applicable only to halide ions. From Pascal's work the values of the susceptibilities of halogen molecules are known. Methods are available for calculating these molecular susceptibilities and also for calculating the susceptibility of a halide ion. On the basis of the ratio $\chi_{M(\text{theor.})}/\chi_{M(\text{exptl.})} = \chi_{\text{ion}(\text{theor.})}/\chi_{\text{ion}(\text{exptl.})}$, Miss Trew derives values for $\chi_{\text{ion}(\text{exptl.})}$.

Most of these methods are reviewed by Miss Trew and she then averages the individual values and obtains the following ionic susceptibilities: $F' = 9.1 \pm 1.8$; $Cl' = 23.4 \pm 1.3$; $Br' = 34.6 \pm 1.6$; $I' = 50.6 \pm 1.6$; $Li' = 1.0$; $Na' = 6.8$; $K' = 14.9$; $Rb' = 22.5$; and $Cs' = 35.0$. The justification for including all the individual values she has used is rather questionable. Experimental confirmation of data is the first step towards settling these difficulties. Then only can some rigorous treatment be applied. Empirical adjusting of values by an arbitrary choice of the susceptibilities of the ions from which other susceptibilities are deduced will never attain the desired objective. After all, L. Pauling⁷² by choosing values of -5.2 and -14.5 for $\chi_{Na'}$ and $\chi_{K'}$, respectively (in each instance numerically 4 units less than the values chosen by Pascal), deduced, from Pascal's data, values for ions of alkali and alkaline-earth salts which were satisfactory for simple ions.

The classical formula of Langevin⁴ for the diamagnetic susceptibility of a spherically symmetrical atom or ion is $\chi = -(e^2/6mc^2)\Sigma\bar{r}^2$, where \bar{r}^2 is the time average of r^2 , the distance of the electron from the nucleus, and the summation is extended over all the circumnuclear electrons. In quantum mechanics this formula also holds but the value of \bar{r}^2 is different. $\Sigma\bar{r}^2$ has been calculated, independently, by J. H. van Vleck⁷³ and L. Pauling;⁷² the latter has calculated a number of ionic susceptibilities but they are, generally, higher than experimental values. D. R. Hartree's⁷⁴ space charge distribution method has been utilised by E. C. Stoner⁷⁵ and G. W. Brindley⁶² but, again, values numerically greater than the experimental values are obtained. J. C. Slater,⁶³ utilising the fact that the nodes in a wave function are unimportant, has shown how wave functions of atoms and ions may be calculated conveniently by neglecting the nodes and taking as the radial part of the wave function of one electron in a symmetrical atom $\psi =$

⁶⁹ *Ann. Physik*, 1935, **24**, 697.

⁷⁰ *Avh. norsk. Vidensk.-Akad. Oslo, Mat.-nat. Kl.*, 1933, No. 9, 21 pp.

⁷¹ *Sci. Rep. Tôhoku Imp. Univ.*, 1932, **22**, 149, 288, 869; and *Rep. Yokohama Tech. Coll.*, 1934, No. 2, 203, 223, 233.

⁷² *Proc. Roy. Soc.*, 1927, **A**, **114**, 181.

⁷³ *Proc. Nat. Acad. Sci.*, 1926, **12**, 662.

⁷⁴ *Proc. Camb. Phil. Soc.*, 1928, **24**, 89, 111.

⁷⁵ *Proc. Leeds Phil. Soc.*, 1929, **1**, 484.

Author.	Li.	Na.	K.	Rb.	Cs.	Mg.	Ca.	Sr.	Ba.	F.	Cl.	Br.	I.	Ref.
<i>Experimental:</i>														
Joos	—	6.5	14.5	—	—	9	9	24	43	11.5	19.5	39.5	60.5	59
Ikenmeyer	4.0	10.4	16.9	31.3	45.75	4.5	11.0	25.4	39.9	13.9	20.4	34.8	49.25	61
Brindley	0.7	5.2	13.5	24.0	36.8	3.8	10.8	19.5	30.0	—	24.0	37.5	55.7	62
Brindley and Hoare	0.7	6.1	14.6	22.0	35.1	4.3	10.7	18.0	29.0	9.4	24.2	34.5	50.6	64
Weiss (Pascal)	—	7.6	16.0	24.3	41.0	—	—	—	—	—	23.1	34.7	49.8	65
” (Hocart)	—	8.2	16.5	—	—	5.2	10.6	18.9	—	—	23.1	33.9	49.5	
” (Reicheneder)	—	—	—	—	—	—	—	—	—	—	23.0	33.6	50.8	68
Abonnenc	2.6	7.5	16.3	25.0	38.3	6.7	11.1	19.9	30.9	7.7	23.1	—	—	
Veiel	3.8	9.0	17.4	—	—	—	12.4	22.5	34.6	—	21.8	33.0	50.8	69
Kido	1.6	7.6	13.6	27.2	41.0	4.3	6.5	15.6	23.6	12.2	22.1	34.7	53.2	70
Trew	1.0	6.8	14.9	22.5	35.0	—	—	—	—	9.1	23.4	34.6	50.6	58
<i>Theoretical:</i>														
Pauling	0.6	4.2	16.7	35	55	3.2	13.3	28	46	8.1	29	54	80	72
Brindley	0.7	5.2	13.5	24.0	36.8	3.8	10.8	19.5	30.0	—	24.0	37.5	55.7	62
Slater	0.7	4.2	14.4	25.8	39.6	3.2	11.4	21.5	33.3	8.3	25.8	40.0	59.8	63
Angus	0.7	3.7	13.1	24.1	37.2	2.9	10.4	20.2	31.6	7.3	22.9	36.7	55.3	57
Brindley	0.9	5.1	13.5	23.6	36.9	—	10.4	18.7	31.9	9.0	23.6	39.7	59.7	77
Mrowka	—	2.9	8.4	27.8	—	3.5	—	18.2	24.0	—	—	—	—	78
Hirone	—	10	18	32	43	5.8	11	23	32.5	—	—	—	—	80
Gombás	—	15	20	28	33	—	17	26	31	—	31	35	39	81

$r^{(n^*-1)}e^{-(Z-s)/n^*r}$, where n^* is the effective quantum number and $(Z - s)$ the effective nuclear charge. Rules are given by Slater for the evaluation of n^* and s , the screening constant, for an electron group. By integration of the wave function $r^2 = (n^*)^2(n^* + \frac{1}{2})(n^* + 1)/(Z - s)^2$ and for each electron in the group $\chi \times 10^6 = -0.807r^2$. By means of this formula values for ionic susceptibilities in better agreement with experimental data are obtained. For many ions an improved value is obtained by a modification of Slater's method proposed by W. R. Angus.⁵⁷ This consists of treating separately s and p electrons having the same principal quantum number. The justification for this procedure has been questioned;⁵⁸ but all these methods are empirical, so criticism can be levelled at each.

A. Heydweiller's refraction data at infinite wave-length⁷⁶ have been used by G. W. Brindley⁷⁷ and B. Mrowka⁷⁸ to obtain χ_M by means of the relationship between χ_M and polarisability.⁷⁹ Values obtained on the basis of the Thomas-Fermi statistics by T. Hirone⁸⁰ and P. Gombás⁸¹ do not agree well with experimental values. From such a diversity of methods a diversity of values is obtained which, at present, cannot be satisfactorily sorted out. The table on p. 36 illustrates these difficulties.

(7) *Applications of Additivity in Simple Molecules*.—In section (6) reference has been made only to ions which have a rare-gas configuration. If it is assumed that diamagnetism is strictly additive, the susceptibilities of other ions can be deduced from measured molecular susceptibilities by subtracting known susceptibilities of other groups. Thus, to find χ of a cation a number of salts are examined and the anionic contributions are subtracted from the molecular susceptibilities. This procedure is of doubtful value because of prevailing uncertainties regarding the true value of simple ions. Some workers use one set of data, some choose another; there is, accordingly, great confusion in the derived quantities and no real basis for comparing them. In the simple form outlined above the method has been employed to ascertain values for the following ions: Bi^{III} ,^{82, 83, 84} Bi^{V} ,⁸⁴ Sb^{III} ,⁸⁴ Sb^{V} ,⁸⁴ Rb^+ ,⁸⁵ Hg^+ and Hg^{++} ,⁸⁶ Sn^{++} and Sn^{IV} ,⁸⁷ Ag^+ and Cu^+ ,⁸⁸ Cd^{++} ,⁸⁹ Tl^+ ,^{58, 83, 90, 91}

⁷⁶ *Physikal. Z.*, 1925, **26**, 526.

⁷⁷ *Physical Rev.*, 1933, **43**, 1030.

⁷⁸ *Z. Physik*, 1933, **80**, 495.

⁷⁹ J. G. Kirkwood, *Physikal. Z.*, 1932, **33**, 57; J. P. Vinti, *Physical Rev.*, 1932, **41**, 813.

⁸⁰ *Sci. Rep. Tôhoku Imp. Univ.*, 1935, **24**, 264. ⁸¹ *Z. Physik*, 1933, **87**, 57.

⁸² (Sir) S. S. Bhatnagar and B. S. Bahl, *Current Sci.*, 1935, **4**, 153, 234.

⁸³ K. Kido, *Sci. Rep. Tôhoku Imp. Univ.*, 1933, **22**, 835.

⁸⁴ V. I. Vaidyanathan, *Indian J. Physics*, 1930, **5**, 559.

⁸⁵ (Sir) S. S. Bhatnagar, M. B. Nevgi, and M. L. Khanna, *J. Indian Chem. Soc.*, 1935, **12**, 799.

⁸⁶ (Sir) S. S. Bhatnagar, M. B. Nevgi, and G. L. Ohri, *Proc. Indian Acad. Sci.*, 1939, **A**, **9**, 86.

⁸⁷ (Sir) S. S. Bhatnagar, M. B. Nevgi, and R. L. Sharma, *J. Indian Chem. Soc.*, 1936, **13**, 273.

⁸⁸ C. Courty, *Compt. rend.*, 1936, **202**, 1929.

⁸⁹ (Miss) W. R. A. Hollens and J. F. Spencer, *J.*, 1934, 1062; 1935, 495.

⁹⁰ (Miss) V. C. G. Trew, *Trans. Faraday Soc.*, 1936, **32**, 1658.

⁹¹ M. B. Nevgi, *J. Univ. Bombay*, 1938, **7**, 19.

NO_3' .⁹² K. Kido⁹³ has combined the subtraction method with a graphical extrapolation method and thereby deduced values for Ti^{IV} , Ce^{IV} , La^{III} , O'' , S'' , ClO_4' , SO_4'' , PO_4''' , PO_3' , and NO_3' ions and, recently, Miss Trew⁵⁸ has used a graphical method to assist in deducing values for NO_3' , CN' , CNO' , CNS' , CO_3'' , SO_4'' , NH_4' , halogenate, and perhalogenate ions. K. Kido⁹³ has derived values for oxy-acid ions and finds that the susceptibility of an ion with a similar co-molecular structure decreases with increase of the nuclear charge on the central atom in the same group and increases with increase of the nuclear charge on the central atom in the same series.

In their work on alkali halides, G. W. Brindley and F. E. Hoare⁶⁴ found that, with the exception of lithium and caesium chlorides, bromides, and iodides, the other crystalline salts were strictly additive within the limits of experimental error. They suggest reasons. In a lithium halide there is a small cation and a relatively large anion. The anions approach closely and the greater electrostatic repulsions produce larger interatomic distances than would normally be expected. The caesium halides, on the other hand, have a different crystal structure from other alkali halides (sodium chloride structure) and this is responsible for their deviation from strict additivity. The same authors⁹⁹ have also pointed out that ammonium iodide, which has the sodium chloride structure, gives the normal value of χ , whereas ammonium chloride and bromide give low values. Solid lithium hydride gives a value about half that calculated, and this is attributed¹ to a factor which, inoperative in isolated ions, introduces in crystals a paramagnetism practically independent of temperature.

In deducing values for the formate, acetate, iodate, nitrite, nitrate, and selenite ions, S. R. Rao and S. Sriraman⁹⁴ found that the values obtained depended on whether they used crystalline salts or aqueous solutions. The susceptibilities in solution were greater than those for the crystalline salt. Similar observations have been reported in respect of metallic halides by K. C. Subramaniam⁹⁵ but, on the other hand—again using metallic halides—M. Flordal and O. E. Frivold⁹⁶ found no substantial difference. The more recent work of F. E. Hoare and G. W. Brindley⁹⁷ conclusively supports the Indian workers and leads to the following conclusions: (i) the susceptibilities of ions in solution are closely additive, (ii) the susceptibility of a large univalent ion in solution is approximately equal to its value in the crystalline state, (iii) the susceptibilities of small and bivalent ions in solution are less than in the crystalline state owing to hydration effects, (iv) the difference between the values in solution ($\chi_{\text{soln.}}$) and in the crystalline state ($\chi_{\text{cryst.}}$), viz., $\chi_{\text{soln.}} - \chi_{\text{cryst.}}$, varies progressively with Cn/R^2 , where n/R^2 is the field at the boundary of the ion and C is the degree of hydration.

⁹² S. P. Ranganadham and M. Qureshi, *Indian J. Physics*, 1940, **14**, 129.

⁹³ *Sci. Rep. Tôhoku Imp. Univ.*, 1932, **21**, 869.

⁹⁴ *Current Sci.*, 1937, **6**, 54; *Phil. Mag.*, 1937, **24**, 1025; *J. Annamalai Univ.*, 1938, **7**, 187.

⁹⁵ *Proc. Indian Acad. Sci.*, 1936, **A**, **4**, 404.

⁹⁶ *Ann. Physik*, 1935, **23**, 425.

⁹⁷ *Trans. Faraday Soc.*, 1937, **33**, 268; *Proc. Physical Soc.*, 1937, **49**, 619.

Very few data exist for salts in non-aqueous solvents. The susceptibilities of mercuric halides in pyridine are less than in the crystalline state,⁸⁶ and O. E. Frivold and H. Sogn⁸⁸ found that susceptibilities of salts in non-aqueous solvents were less than in aqueous solution.

Calculated values of χ_A are for isolated, free atoms or ions. Measured values are for combined atoms, and F. W. Gray and his collaborators postulate that experimental values should be less than the calculated values (Pauling⁷²) and that the difference is due to depression of diamagnetism resulting from bond formation. Estimates of the magnitude of bond depressions were made for a large number of compounds² before a new and intricate technique was published by F. W. Gray and J. H. Cruickshank³ which may be summarised as follows. Selecting Pauling's⁷² method of calculating ionic susceptibilities, they modify it so as to calculate the susceptibility of an atom which is not exhibiting its extreme values of positive or negative valency corresponding with inert-gas structures. For example, with carbon they calculate values for C^{+4} , C^{+3} , C^{+2} , C^{+1} , C^0 , C^{-1} , C^{-2} , C^{-3} , and C^{-4} . To each atom in a molecule residual charges are assigned on the basis of dipole moments of links, Δe , the residual charge being equal to the bond moment/internuclear separation. These residual charges represent the fraction of time spent in a particular valency state by a particular atom. Thus, since the residual charges on carbon and hydrogen in a C-H bond are, respectively -0.04 and $+0.04$, the CH_2 group is $H^{\pm 0.04} \overset{\overset{+0.04}{|}}{\underset{\underset{-0.08}{|}}{C}} H^{+0.04}$. The theoretical diamagnetic susceptibility of this group is computed as follows: the carbon atom is 0.08 of the time C^{-1} and 0.92 of the time C^0 , and analogously for each hydrogen; therefore, $\chi_M(\text{theor.}) = 0.08\chi_{C^{-1}} + 0.92\chi_{C^0} + 2(0.04\chi_{H^{+1}} + 0.96\chi_{H^0}) = -14.90$. The experimental value (Pascal) is -11.86 and the difference, -3.04 , is the depression arising from one C-C single bond and two C-H bonds. Depressions for a large number of bonds of different types have been computed, and the values are used to interpret the diamagnetic measurements and to discuss the molecular configuration and resonating species of benzene, naphthalene, the carboxyl group, water, and hydrogen peroxide;³ urea and its derivatives;⁴ organic sulphur compounds;⁵ and derivatives of SO_4'' , S_2O_3'' , SO_3'' , and S_2O_2'' radicals.⁶ The agreement between experimental values and calculated values is astonishingly close. The method involves a knowledge of screening constants, bond moments, and internuclear distances, quantities which are not known for very many bonds and, even when known, are not known with complete certainty. In the discussions of molecular structure more attention might have been paid to researches on molecular structure by other and

⁸⁶ *Ann. Physik*, 1935, **23**, 413.

⁸⁸ *Nature*, 1935, **100**, 473.

¹ S. Freed and H. G. Thode, *J. Chem. Physics*, 1935, **3**, 212.

² (a) F. W. Gray and J. Farquharson, *Phil. Mag.*, 1930, **10**, 191; (b) F. W. Gray and J. Dakers, *ibid.*, 1931, **11**, 81, 297; (c) J. Farquharson, *ibid.*, 1932, **14**, 1003.

³ *Trans. Faraday Soc.*, 1935, **31**, 1491. ⁴ A. Clow, *ibid.*, 1937, **33**, 381.

⁵ A. Clow and J. M. C. Thompson, *ibid.*, p. 894.

⁶ A. Clow, H. M. Kirton and J. M. C. Thompson, *ibid.*, 1940, **36**, 1018.

more firmly established methods. The existence of bond depressions is indisputable; they are implied in Pascal's corrections although he makes, unlike Gray and his collaborators, no adjustments for single bonds. Miss Trew⁵⁸ has recently published values, deduced by a different method, for the Cl-O, Br-O, and I-O bonds. Likewise, the variability of the valency of certain atoms has been recognised for a long time and other attempts to evaluate the appropriate susceptibilities have been made.⁷

M. Prasad and S. S. Dharmatti have recently published data on compounds of selenium,⁸ tellurium,⁹ and sulphur¹⁰ which they interpret in terms of bi-, quadri-, and sexa-valent Group VI atoms and for each state deduce susceptibilities, using a modification of Angus's method.⁵⁷ The compounds yield experimental values in reasonable agreement with the calculated values. K. Kido has also derived values for "intermediate" valencies of atoms from his ionic values and applies them to aliphatic compounds^{11a} and to mono- and di-substituted derivatives of benzene.^{11b}

Summation of Pascal's values has yielded results in agreement with measured data in many instances and has been widely adopted. G. B. Bonino and R. Manzoni-Ansidei¹² use it with success for thiophen, furan, pyrrole, and their derivatives, and it yields values in excellent accord with experimental data on $\omega\omega'$ -phenylpolyenes¹³ and the diamagnetic hexa-arylethanes.¹⁴ Its applications to inorganic compounds have been equally successful. It has aided in investigations which have shown the non-existence of single-electron links in dimethyltellurium halides¹⁵ and in basic beryllium acetate and higher analogues;¹⁶ in demonstrating the non-existence of cadmous compounds;⁸⁹ and in the study of rhenium compounds¹⁷—to cite only a few random examples.

This variety of treatment betokens the present unhealthy state of the subject. Much of the difficulty will remain until accurate and independently confirmed experimental values are available through which generalised treatments can be accomplished. Then, and only then, will it be possible for diamagnetism to occupy that important place among the methods of determining molecular structure which many feel it should.

(8) *Polymerisation*.—In 1936 two papers appeared dealing with the changes occurring during and after polymerisation. (Sir) S. S. Bhatnagar, M. B. Nevgi, and R. N. Mathur¹⁸ reported a decrease in diamagnetism of a

⁷ See, e.g., M. B. Nevgi, *J. Univ. Bombay*, 1938, **7**, 82.

⁸ *Proc. Indian Acad. Sci.*, 1940, **A**, 12, 185.

⁹ *Ibid.*, p. 212.

¹⁰ *Ibid.*, 1941, **A**, 13, 359.

¹¹ (a) *Sci. Rep. Tôhoku Imp. Univ.*, 1936, Honda Anniversary Vol., p. 329; (b) *ibid.*, 1936, **24**, 701.

¹² *Ric. sci.*, 1936, **7**, Reprint.

¹³ E. Müller and I. Dammerau, *Ber.*, 1937, **70**, 2561.

¹⁴ E. Müller and W. Kruck, *ibid.*, 1938, **71**, 1778.

¹⁵ (Sir) S. S. Bhatnagar and T. K. Lahiri, *Z. Physik*, 1933, **84**, 671.

¹⁶ W. R. Angus and J. Farquharson, *Proc. Roy. Soc.*, 1932, **A**, 136, 579.

¹⁷ N. Perakis and L. Capatos, *J. Phys. Radium*, 1935, **6**, 462; W. Klemm and G. Frischmuth, *Z. anorg. Chem.*, 1937, **230**, 220.

¹⁸ *Z. Physik*, 1936, **100**, 141.

number of compounds, including anthracene and furfuraldehyde, on polymerisation. The other paper, by J. Farquharson,¹⁹ discusses the polymerisation of $\beta\gamma$ -dimethylbutadiene, cyclopentadiene, cyanogen chloride, and nitrosobenzene and the molecular susceptibility of a n -polymeride of X is given by $\chi_M = n\chi_X + (n - 1)\lambda$, where λ is the correction factor for the new chemical bonds, these being assumed to be all of one type. The disappearance of a double bond in the polymerisation of $\beta\gamma$ -dimethylbutadiene causes, as predicted from Pascal's correction factors, a progressive increase in χ with time. This enables Farquharson to combine his magnetic data with existing chemical evidence and to calculate the mean molecular weight under different conditions. A later paper²⁰ reports that in the uncatalysed polymerisation of dimethylbutadiene χ decreases for the first 3 hours and then increases. This is attributed to the preliminary stage of polymerisation being the formation of paramagnetic free radicals of the butadiene with one electron missing, and their concentration has been calculated. Although double bonds also disappear in the polymerisation of cyclopentadiene, the anticipated increase in diamagnetism is not found; instead there is a fall which, it is tentatively suggested, may be due to the bridged ring of the polymeride. The ring closure which accompanies the polymerisation of cyanogen chloride to cyanuric chloride may be responsible, as well as the change from C:N to C:N bonds, for the marked diminution in diamagnetism which is encountered. More recently²¹ it has been found that ring formation in hydrogen-bonded structures—formed by either inter- or intra-molecular hydrogen bonds—of benzoic or monohydroxybenzoic acids in solvents of different proton-attracting powers leads to a value of χ numerically less than the anticipated additive value and diminishing as the concentration of solute increases. On the other hand, when an "open" addition compound is formed by intermolecular hydrogen bonding between solute and solvent χ_{solute} increases with solute concentration.

J. Farquharson²² has used magnetic measurements and a modification of his earlier formula for χ of the polymeride to evaluate the diamagnetic susceptibility of the recurring $-\text{CH}_2\text{O}-$ group in polyoxymethylene diacetates and to calculate the number of these groups in α - and β -polyoxymethylenes. This treatment yields an explanation of the earlier results of W. Good²³ on α -, β -, γ -, and δ -polyoxymethylenes.

Dianthracene is produced by photopolymerisation, in a vacuum, of anthracene in the solid state or in benzene solution, and the net result is that the anthracene molecule loses two double bonds and gains a bridged four ring. This is accompanied by a fall in diamagnetism according to (Sir) S. S. Bhatnagar, P. L. Kapur, and (Miss) G. Kaur,²⁴ who have also studied the polymerisation of styrene in oxygen and in a vacuum.²⁵

¹⁹ *Trans. Faraday Soc.*, 1936, **32**, 219.

²⁰ J. Farquharson and (Miss) P. Ady, *Nature*, 1939, **143**, 1067.

²¹ See ref. (19), p. 29.

²² *Trans. Faraday Soc.*, 1937, **33**, 824.

²³ *J. Roy. Tech. Coll. Glasgow*, 1931, **2**, 401.

²⁴ *Proc. Indian Acad. Sci.*, 1939, **A**, **10**, 468.

²⁵ *J. Indian Chem. Soc.*, 1940, **17**, 177.

Diamagnetic measurements in the temperature range -40° to $+10^{\circ}$ have been invoked by J. Farquharson, C. F. Goodeve, and F. D. Richardson²⁶ to determine the concentrations of ClO_3 in mixtures of ClO_3 and Cl_2O_6 and, hence, the corresponding equilibrium constants. ClO_3 is an odd-electron molecule and is, therefore, paramagnetic; its susceptibility was calculated from the van Vleck formula. Since all the mixtures were diamagnetic it follows that Cl_2O_6 is diamagnetic and must, therefore, be in the 1Σ state.

Although it was impossible by magnetic measurements to differentiate between the odd-electron (KO_2) and the even-electron (K_2O_4) formulation,²⁷ the following formulæ have been adduced as preferable to KBH_3 , $\text{KBH}_2\cdot\text{OH}$, and NaSO_2 , respectively: $\text{K}_2\text{B}_2\text{H}_6$,²⁸ $\text{K}_2\text{B}_2\text{H}_4(\text{OH})_2$,²⁸ and $\text{Na}_2\text{S}_2\text{O}_4$.²⁹

(9) *Addition Compounds and Complexes*.—Although the addition compounds formed between *m*-dinitrobenzene or picric acid and amines or hydrocarbons were found, in the solid state, to be more diamagnetic than was to be expected from additivity relationships,³⁰ the same compounds exhibit less diamagnetism in benzene solution than in the solid state.³¹ KHgI_3 (solid³⁶ and in solution³²), $\text{NH}_4\text{HgI}_3\cdot 2\text{H}_2\text{O}$,³⁶ K_2HgI_4 and Na_2HgI_4 ³² have χ values approximately equal to those obtained by additivity, whereas Ag_2HgI_4 ³³ gives a value about 30% less than the additivity value.

Many complexes of transition elements containing CO or CN groups exhibit diamagnetism, *e.g.*, carbonyls. Recent work has shown that the following are diamagnetic: $\text{K}_4\text{Mo}(\text{CN})_8$,³⁴ $\text{KTI}_3[\text{ReO}_2(\text{CN})_4]$,³⁵ $[\text{Re}(\text{NH}_3)_6]\text{Cl}_5$,³⁵ $[\text{Fe}(\text{NO}_2)_6]'''$ and $[\text{Co}(\text{NO}_2)_6]'''$ are diamagnetic, but $[\text{Co}(\text{NO}_2)_6]''''$ and $[\text{Cu}(\text{NO}_2)_6]''''$ are paramagnetic.³⁶ Diamagnetic $\text{Ag}_2[\text{Co}(\text{H}_2\text{O})(\text{CN})_5]$ changes colour from yellow to blue and becomes feebly paramagnetic on dehydration.³⁷ The diamagnetism of nickel complexes of diazoaminobenzene and 4 : 4'-dimethyldiazoaminobenzene indicates that they contain square co-ordinated nickel atoms and that the triazene group functions as a chelate group.³⁸

(10) *Binary Mixtures*.—From 1918, when A. W. and A. W. Smith³⁹ showed that the mixtures $\text{COMe}_2\text{-H}_2\text{O}$, $\text{AcOH-C}_6\text{H}_6$, and $\text{COMe}_2\text{-EtOH}$

²⁶ *Trans. Faraday Soc.*, 1936, **32**, 790.

²⁷ W. Klemm and H. Sodomann, *Z. anorg. Chem.*, 1935, **225**, 273; E. W. Neumann (*J. Chem. Physics*, 1934, **2**, 31) reported that the superoxide was paramagnetic.

²⁸ L. Klemm and W. Klemm, *Z. anorg. Chem.*, 1935, **225**, 258.

²⁹ L. Klemm, *ibid.*, 1937, **231**, 136.

³⁰ (Sir) S. S. Bhatnagar, M. J. Verma, and P. L. Kapur, *Indian J. Physics*, 1935, **9**, 131.

³¹ (Sir) S. S. Bhatnagar, M. B. Nevgi, and G. Tuli, *ibid.*, p. 311.

³² F. Gallais, *Compt. rend.*, 1937, **205**, 1052.

³³ *Idem*, *ibid.*, 1932, **195**, 1390.

³⁴ W. A. Rawlinson, *J. Proc. Austral. Chem. Inst.*, 1941, **8**, 42.

³⁵ W. Klemm and G. Frischmuth, *Z. anorg. Chem.*, 1937, **230**, 220.

³⁶ L. Cambi and A. Ferrari, *Gazzetta*, 1935, **65**, 1162.

³⁷ P. Ray and N. K. Dutt, *Current Sci.*, 1937, **5**, 476.

³⁸ F. P. Dwyer and D. P. Mellor, *J. Amer. Chem. Soc.*, 1941, **63**, 81.

³⁹ *J. Amer. Chem. Soc.*, 1918, **40**, 1218.

obeyed the additivity relationship, until about 1931 little attention was paid to the variation of χ with the concentration of the components of a binary mixture. Since then a number of papers have appeared⁴⁰ which indicate that the additivity relationship holds approximately; there are slight deviations from linearity attributed to co-ordination and de-association effects by some workers,^{40c, m} and to the mutual influence of electrically polar molecules by Ranganadham,^{40e} although Rao and Narayanaswamy,⁴⁰ⁿ from an investigation of the susceptibilities of mixtures of formic and acetic acids with methyl and ethyl alcohol, acetone, and ethyl ether, maintain that the slight deviations are independent of the electric moments of the components of the mixtures.

On the basis of additivity, aqueous solutions of formic acid show small but definite diminution in diamagnetism with maximum deviation at 70% of acid, which may be due to the formation of the monohydrate or to the dimerisation of the acid.⁴¹ Acetic acid solutions, on the other hand, obey the additivity rule.^{14 (p. 28), 39, 40n} With aqueous solutions of inorganic acids irregularities in the χ -concentration curves occur which are interpreted as due to formation of hydrates. For hydrogen chloride, J. Farquharson⁴² found a number of maxima corresponding with all the hydrates from 3 to 10H₂O, but A. F. Scott and C. M. Blair⁴³ could find no maximum or minimum. Farquharson⁴² reports irregularities corresponding with H₂SO₄.H₂O and H₂SO₄.3H₂O, to which P. S. Varadachari^{14 (p. 28)} has added H₂SO₄.18H₂O, H₂SO₄.6H₂O, and 2H₂SO₄.H₂O; but B. N. Rao⁴⁴ could find none of these and reports only H₂SO₄.2H₂O. The departures from linearity in the curves for nitric acid correspond with the four hydrates HNO₃.50H₂O, HNO₃.6H₂O, HNO₃.4H₂O, and 2HNO₃.5H₂O.⁴⁵ Recently M. R. Nayar and N. K. Mundle⁴⁶ have examined solutions of iodic acid (0.01—1.0N) and found breaks in the χ -N curves at 0.04 and 0.08N.

(11) *Gases*.—Molecules with an even number of circumnuclear electrons are diamagnetic if they are in a ¹ Σ state. Oxygen, although it contains an even number of electrons, is in a ³ Σ state and is, consequently, paramagnetic. Nitrogen mono- and di-oxide and chlorine di- and tri-oxide are paramagnetic by virtue of their unbalanced structure resulting from at

⁴⁰ (a) H. Buchner, *Nature*, 1931, **128**, 301; (b) J. Farquharson, *ibid.*, 1932, **129**, 25; (c) J. E. Garssen, *Compt. rend.*, 1933, **196**, 541; (d) K. Kido, *Sci. Rep. Tôhoku Imp. Univ.*, 1932, **21**, 385; (e) S. P. Ranganadham, *Indian J. Physics*, 1931, **6**, 421; (f) S. R. Rao, *ibid.*, 1933, **8**, 483; (g) S. R. Rao and G. Sivaramakrishnan, *ibid.*, 1931, **6**, 509; (h) S. R. Rao and P. S. Varadachari, *Proc. Indian Acad. Sci.*, 1934, **A**, **1**, 77; (i) C. Salceanu and D. Gheorghiu, *Compt. rend.*, 1935, **200**, 120; (j) S. Seely, *Physical Rev.*, 1936, **49**, 812; (k) J. F. Spencer and (Miss) V. C. G. Trew, *Nature*, 1936, **138**, 974; (l) (Miss) V. C. G. Trew and J. F. Spencer, *Trans. Faraday Soc.*, 1936, **32**, 701; (m) (Miss) V. C. G. Trew and (Miss) G. M. C. Watkins, *ibid.*, 1933, **29**, 1310; (n) S. R. Rao and A. S. Narayanaswamy, *Proc. Indian Acad. Sci.*, 1939, **A**, **9**, 35; see also Ref. 56.

⁴¹ S. R. Rao and S. Sriraman, *J. Annamalai Univ.*, 1938, **7**, 187. See also Ref. 40n.

⁴² *Phil. Mag.*, 1931, **12**, 283.

⁴³ *J. Physical Chem.*, 1933, **37**, 475.

⁴⁴ *Proc. Indian Acad. Sci.*, 1936, **A**, **3**, 188.

⁴⁵ S. P. Ranganadham and M. Qureshi, *Z. physikal. Chem.*, 1936, **B**, **33**, 290.

⁴⁶ *Current Sci.*, 1941, **10**, 76.

least one electron not being paired. However, if such molecules undergo dimerisation the dimeride will contain an even number of circumnuclear electrons and will be diamagnetic, *e.g.*, Cl_2O_6 ²⁶ and N_2O_4 ,^{47, 64} or feebly paramagnetic.

Experimental difficulties are most probably the cause of the limited amount of data in this field and particularly in respect of organic vapours. The experimental procedure of J. Schur⁴⁶ was the most promising, and by it, the constancy of χ for both the liquid and the gaseous state of carbon disulphide, benzene,⁴⁸ and bromine⁴⁹ has been established. Much more work in this direction is required to adjudge the existing conflicting evidence with regard to the probable alteration in χ on vaporisation.

The values of χ obtained experimentally and theoretically for the rare gases, hydrogen, and an isosteric pair are collected in the table below.

Author.	He.	Ne.	A.	$-\chi \times 10^6.$		H ₁ .	N ₂ .	CO.	Ref.
				Kr.	Xe.				
<i>Experimental :</i>									
Wills and Hector	1.95					3.96			50*
Hector	1.88	6.66	18.1				11.83		51*
Abonnenc			19.2	29.2	44.1				52*
Gerlach			19.7						53*
Havens	1.91	7.65	19.2			4.01	11.94		54*
Mann		6.75	19.5	28.0	42.4				55*
Jaanus and Schur								11.8	56*
<i>Theoretical :</i>									
Pauling	1.54	5.7	21.5	42	66				72
Slater	1.68	5.7	18.9	31.7	48.0				63
Angus	1.68	5.1	16.95	29.3	44.8				57
Brindley	1.97	6.1	16.7	29.3	45.5				77
Vinti.....	1.97	6.97							57*
van Vleck and Frank						4.2			58*
Wang	1.53					4.71			59*
Wick						3.96			60*
Witmer						3.87			61*
Honda and Hirone.....						3.85			62*

* References denoted thus relate to the second one so numbered.

By means of the methods discussed in section (6) for the calculation of the susceptibility of an ion with a rare-gas configuration, values of χ for rare gases can be obtained. The agreement with experimental data is not particularly good for any method; but the measured values are in tolerable agreement with each other. Comparison with the experimental data for the rare gases must surely be the criterion by which a method of calculation can be judged, and the failure of Pauling's method in this respect suggests that it is unsuitable for use in calculating ionic susceptibilities. Nevertheless, as has already been pointed out, Gray *et al.*³⁻⁶ found that values calculated

⁴⁷ G. G. Havens, *Physical Rev.*, 1932, **41**, 337.

⁴⁸ *Physikal. Z. Sovietunion*, 1937, **11**, 194.

⁴⁹ J. Schur and R. Jaanus, *ibid.*, 1935, **7**, 501.

⁵⁰ *Physical Rev.*, 1924, **23**, 209.

⁵¹ *Ibid.*, 1924, **24**, 418.

⁵² *Compt. rend.*, 1939, **208**, 986.

⁵³ *Z. Physik*, 1933, **85**, 545.

⁵⁴ *Physical Rev.*, 1932, **41**, 337.

⁵⁵ *Z. Physik*, 1936, **98**, 548.

⁵⁶ *Physikal. Z. Sovietunion*, 1935, **7**, 19.

⁵⁷ *Physical Rev.*, 1933, **41**, 813.

by a method basically related to Pauling's agreed very closely with their measured values. To reconcile these opposing facts most satisfactorily would involve remeasurement of the rare gases; confirmation of the existing values would indicate a fundamental error in the interpretation of the data on the polyatomic molecules and necessitate a readjustment of ideas regarding bond diamagnetism.

Quantum-mechanical treatment is possible only with the simplest systems and for helium and hydrogen yields values ⁵⁸⁻⁶² which are, on the whole, acceptably close to the experimental data.

It is noteworthy that the isosteric molecules, carbon monoxide and nitrogen, have identical susceptibilities. This is in line with other physical properties of the pair. T. Soné found values very close to each other for carbon dioxide ⁶³ and nitrous oxide, ⁶⁴ another isosteric pair. Unfortunately, his method appears to be at fault because his value for carbon dioxide is -18.61 , which is considerably less than -20.9 found by other investigators. ⁶⁵ No reliable comparative datum for nitrous oxide exists.

(12) *Miscellaneous*.—An interesting application to molecular structure has been made recently by R. W. Asmussen. ⁶⁶ On X-ray evidence in compounds of the type Rb_2SbCl_6 all antimony atoms are equivalent. The simplest explanation would be to assign a valency of four to antimony, which would then possess an odd-electron structure and, consequently, would confer paramagnetism on the molecule. From measurements on eight compounds, all of which are diamagnetic, it is concluded that these compounds do not contain Sb^{IV} but, probably, alternate Sb^{III} and Sb^{V} . These conclusions support the earlier suggestion of N. Elliott ⁶⁷ that $(\text{NH}_4)_2\text{SbBr}_6$ contained no single molecules but only dimerides.

Magnetic measurements by P. W. Selwood have recently shown that it is unlikely that hexaphenyldigermane ⁶⁸ is dissociated in the solid state or to more than 20% in benzene at 25° , whilst for hexaphenyldiplumbane ⁶⁹ the upper limit of dissociation to triphenyl-lead in benzene is 1.4% and in the solid state 0.1% at temperatures from 30° to 80° . Trimethyltin and tri-cyclohexyl-lead do not exist in the monomeric form in dilute benzene solution. ⁷⁰ These results cast doubt on the existence of long-life organometallic free radicals. The fact that the vapour of calomel is diamagnetic between 250° and 375° excludes the formula HgCl . ⁷¹

⁵⁸ *Proc. Nat. Acad. Sci.*, 1929, **15**, 539.

⁵⁹ *Ibid.*, 1927, **13**, 798.

⁶⁰ *Z. Physik*, 1933, **85**, 25; *Nuovo Cim.*, 1933, **10**, 118.

⁶¹ *Physical Rev.*, 1935, **48**, 380.

⁶² *Z. Physik*, 1933, **84**, 208.

⁶³ *Sci. Rep. Tôhoku Imp. Univ.*, 1919, **8**, 115.

⁶⁴ *Ibid.*, 1922, **11**, 139.

⁶⁵ E. Lehrer, *Ann. Physik*, 1926, **81**, 229; S. R. Rao and G. Sivaramakrishnan, *Proc. Physical Soc.*, 1934, **46**, 318; and Ref. 54 (p. 33).

⁶⁶ *Z. Elektrochem.*, 1939, **45**, 698.

⁶⁷ *J. Chem. Physics*, 1934, **2**, 419.

⁶⁸ *J. Amer. Chem. Soc.*, 1939, **61**, 3168.

⁶⁹ R. Preckel and P. W. Selwood, *ibid.*, 1940, **62**, 2765.

⁷⁰ H. Morris and P. W. Selwood, *ibid.*, 1941, **63**, 2509.

⁷¹ P. W. Selwood and R. Preckel, *ibid.*, 1940, **62**, 3055.

G. N. Tyson and S. C. Adams ⁷² prove that the salicylaldehyde complex of nickel is planar and diamagnetic whereas, although planar, the cupric complex is paramagnetic. The paramagnetic salicylaldehyde complexes of nickel(II) and cobalt(II) are tetrahedral but the corresponding cupric complex is planar. Most probably cupric disalicylaldehyde is also planar.⁷³

C. M. Beeson and C. D. Coryell,⁷⁴ from measurements on gaseous nitrosyl chloride at 25°, concluded that it was diamagnetic and in a 1Σ state; it resembles sulphur dioxide in physical properties. This, and the fact that the χ values for additive compounds of nitrosyl chloride with inorganic chlorides indicate that it is diamagnetic, led R. W. Asmussen ⁷⁵ to postulate resonance between the forms $\text{Cl}-(\text{NO})^+$, $\text{Cl}-\text{N}=\text{O}$, and $\text{Cl} \rightleftharpoons \text{N} \rightarrow \text{O}$. J. A. A. Ketelaar ⁷⁶ showed, on electron-diffraction evidence, that there is resonance between the two structures, $\text{Cl}-\text{N}=\text{O}$ and $\text{Cl}-(\text{NO})^+$.

An examination of solid sodium and potassium salts of acetic, propionic, and butyric acids has shown that the experimental values agree with those calculated. On the other hand, the corresponding salts of palmitic, stearic, oleic, and myristic acids give values less than the calculated values; this is attributed by M. B. Nevgi ⁷⁷ to the formation of micelles of large particles of colloidal dimensions.

In view of the limitations necessarily imposed on the size of a Report of this kind it has been decided to omit certain topics in spite of their intrinsic interest and importance; notable omissions are anisotropy and the diamagnetism of metals, with the influences exerted by pretreatment of the samples, particle size, and crystal structure.

W. R. A.

4. MOLECULAR SPECTRA AND THERMODYNAMICS.

In recent years thermodynamics has received considerable help from accurate spectroscopic measurements, since the evaluation of the energy levels occupied by molecules enables specific heats to be computed. Most of the data come from infra-red and Raman spectra, and therefore in the following survey little reference is made to ultra-violet spectra, which were reviewed two years ago.¹

Internal Rotation in Molecules.—The application of physicochemical methods to the study of internal rotation in molecules has been mentioned in previous Reports.² During recent years information about this has accumulated rapidly. Some advance has come from the measurement of dipole moments and the effect of temperature upon them,³ and from X-ray and electron-diffraction measurements, but the main progress has been made by the use of optical methods, and the correlation of optical data with other physicochemical results.

⁷² *J. Amer. Chem. Soc.*, 1940, **62**, 1228.

⁷³ G. N. Tyson and R. E. Vivian, *ibid.*, 1941, **63**, 1403.

⁷⁴ *J. Chem. Physics*, 1938, **6**, 656.

⁷⁵ *Z. anorg. Chem.*, 1939, **243**, 127.

⁷⁶ *Atti X Cong. intern. Chim.*, 1938, II, 301.

⁷⁷ *J. Univ. Bombay*, 1938, **7**, 74.

¹ *Ann. Reports*, 1939, **36**, 47.

² *Ibid.*, 1938, **35**, 42.

³ G. I. M. Bloom and L. E. Sutton, *J.*, 1941, 727.

In a molecule such as ethane, rotation of one end of the molecule with respect to the other will lead to two sets of three identical positions. Only one form of ethane is known. Hence, either the potential barrier resisting the torsion must be very small, so that effectively free rotation occurs, or it must be high, leading to an effectively fixed relative orientation of the two end groups. In all such cases the state of affairs can only be understood completely by a knowledge of the potential energy as a function of the azimuthal angle of internal rotation, which gives the height of the barriers (U_0). If kT is much greater than U_0 we have free rotation, and if kT is less than U_0 we have a torsional oscillation, and the problem is therefore essentially a determination of the heights of the restricting barrier potentials. A comparison of these barriers in different compounds should throw light on the causes of such restriction potentials. Herein lies the real reason for the recent advances, since estimates of the barriers in a series of related molecules are now available, and although in some respects the values determined must still be accepted with reserve, it is probable that refinement of the relevant theory will soon lead to important progress. One factor which is directly relevant to the understanding of the origin and size of potentials restricting the rotation about bonds is the mutual influence of neighbouring non-bonded atoms upon each other. For instance, if in ethane the hydrogen atoms of different methyl groups had a mutual attraction, the stable structure might be expected to be that in which the three pairs of hydrogen atoms are opposite each other, i.e., one end of the molecule "eclipsing" the other, with a symmetry of the class D_{3h} . On the other hand, repulsive forces between the pairs of hydrogen atoms will lead to a "staggered" structure (symmetry D_{3d}), obtained from the eclipsed form by rotation of one methyl group through 60° with respect to the other methyl group. There has consequently been much discussion about the relative stability of the eclipsed and the staggered configuration, and this relative stability affects the structure of certain molecules in other ways discussed below.

Apart from less studied phenomena such as the Kerr effect, there are three principal optical approaches to this question, viz., (1) the use of Raman spectral data, (2) the analysis of the rotational fine structure of infra-red vibrational absorption bands, and (3) the comparison of thermodynamical properties of molecules calculated statistically, using the energy levels determined spectroscopically, with the values of these properties determined by other experimental methods. Of these three independent lines of work, the third has been the most productive, and will be considered first.

The thermodynamical-statistical procedure may be summarised as follows.⁴ It is first necessary to determine, by a correlation of data from the infra-red and Raman spectra, the vibration frequencies of the molecule concerned, as regards both magnitude and assignment to vibrational types. Values for the moments of inertia must then be obtained, either from the

⁴ See S. Glasstone, *Ann. Reports*, 1935, 32, 66; L. Kassel, *Chem. Reviews*, 1936, 18, 277; R. H. Fowler and E. A. Guggenheim "Statistical Thermodynamics," Cambridge, 1940.

rotational structure of vibrational absorption bands, or by other methods such as electron diffraction. These either lead directly to the values of the rotational energy levels, or in more complex cases of asymmetrical rotators to less specific but nevertheless adequate data about these levels, since the total rotational partition function for molecules at reasonable temperatures is given by an explicit function of the moments of inertia. Similar knowledge of the electronic energy levels above the electronic ground state may also be required, although as a rule the comparatively high value of all such levels above the lowest makes this information unnecessary. The molecular partition function, $Q = \sum p_i e^{-E_i/kT}$, in which p_i is the degeneracy of an energy level E_i , may then be calculated. Actually, the total partition function $Q = Q_{\text{el.}} Q_{\text{transl.}} Q_{\text{vib.}} Q_{\text{rot.}}$, and since it appears in the expressions for all the thermodynamic functions as $\log Q$, the several contributions from the different types of energy are additive. As a rule $Q_{\text{el.}} = 1$, and at reasonably high temperatures for polyatomic molecules $Q_{\text{transl.}} = (2\pi M)^{3/2} k^{5/2} T^{5/2} / h^3 P N^{3/2}$, in which M is the molecular weight, P the pressure, N the Avogadro number, and k and h the Boltzmann and the Planck constant respectively. Also $Q_{\text{rot.}} = 8\pi^2 (2\pi kT)^{3/2} \sqrt{I_A I_B I_C} / h^3 \sigma$ in which I_A , I_B , and I_C are the principal moments of inertia, and σ the "symmetry number," i.e., the number of indistinguishable configurations which may be arrived at by rotations of the molecule in space; and $Q_{\text{vib.}} = \prod (1 - e^{-h\nu/kT})^{-1}$, a product which is taken over all the vibrational frequencies ν . By statistical methods the total partition function can now be related directly to the various thermodynamic functions. The expressions for the molar entropy, free energy, and specific heat at constant pressure are as follows:

$$\begin{aligned} S &= R \ln Q + RT \cdot d \ln Q / dT \\ G &= -RT \ln Q \\ C_p &= RT^2 d^2 \ln Q / dT^2 + 2RT \cdot d \ln Q / dT \end{aligned}$$

Reduced expressions for S , G , and C_p as functions only of the several molecular magnitudes after numerical substitution of the fundamental constants have been given by E. B. Wilson.⁵ It is customary in practice to calculate the "virtual" entropy, which ignores any contribution of nuclear spin effects to the partition function, since for all molecules other than hydrogen they are negligible at reasonable temperatures.

The same thermodynamic quantities can, on the other hand, be measured, the specific heat directly, the entropy by integration of a C_p - $\ln T$ plot, the third law of thermodynamics being assumed, and due allowance made for changes in state and any "order-disorder" phenomena in the solid state, and the free energy from the experimental determination of equilibrium constants. The measured values, which must be referred to some standard state such as one atmosphere pressure, will in general require correction for non-ideality of the gas laws applying to the real vapours, for which purpose some knowledge of the equation of state or virial coefficients is required.

⁵ *Chem. Reviews*, 1940, 27, 17.

Suitable approximations for the latter can be derived if the critical data are known.

It has long been known that satisfactory agreement exists between the calculated and the measured thermodynamic properties for many simple molecules having a rigid framework. This indicates the validity of assuming the third law of thermodynamics as well as the general correctness of the statistical method, which has therefore been used extensively for calculating unknown magnitudes. Discrepancies were noticed, however, with other molecules, such as those in which a torsional motion, or double minimum potential energy function (*e.g.*, invertable pyramid) may occur. These discrepancies were, moreover, greater than those to be expected because of the anharmonic character of vibrations, and must be explained in some other way. If a twisting vibration of an essentially rigid framework passes into a free internal rotation, an alteration will be necessary in both the vibrational and the rotational partition functions. The torsional vibration frequency is then omitted from the product in calculating $Q_{\text{vib.}}$, and a further Q for the internal rotation is introduced given by $2\pi(2\pi I kT)^{1/2}/nh$; I is the reduced moment of inertia of the two mutually rotating end groups, and n the internal symmetry number defined below. If the torsional motion is neither free nor vibrational, but intermediate in character, the form of the partition function $Q_{\text{rot.}}$ cannot be given explicitly, but will depend on several factors such as the form of the function relating potential energy and azimuthal angle of rotation, and upon the absolute height of the restricting potential barriers. K. S. Pitzer, first gave a fundamental treatment of this problem,⁶ assuming a potential barrier function of the type $U = U_0/2(1 - \cos n\theta)$. He has given tables for S , G , and C_p from which for given values of U_0 , I , and n the contributions towards the several properties can be read off. This makes it possible to reverse the procedure and, from the disparity between observed and calculated values, to estimate the value of U_0 which will give agreement. This method has been used by most workers. B. L. Crawford⁷ has attempted to extend and improve Pitzer's theory, by considering the general system of several tops attached to a rigid framework, and has suggested that in some cases calculations by Pitzer's method may lead to serious errors in the values determined for U_0 . This argument has been questioned by K. S. Pitzer and W. D. Gwinn,⁸ who draw attention to several defects in Crawford's treatment. Neither theory appears yet to be entirely satisfactory, if for no other reason than that there is uncertainty in the form of the function relating potential energy and azimuthal angle of rotation, but the main principles of the method can be regarded as established. Of the various properties which may be used in the comparison, the specific heat seems to be the most sensitive, but if this is used rather than entropy, there must be complete certainty about the values of the molecular vibration frequencies.

In considering experimental results, we take the classical case of ethane

⁶ *J. Chem. Physics*, 1937, 5, 469.

⁷ *Ibid.*, 1940, 8, 273; see also B. L. Crawford and E. B. Wilson, *ibid.*, 1941, 9, 323.

⁸ *Ibid.*, p. 485.

first. Earlier specific-heat measurements by Eucken and the analysis of the vibrational spectrum by E. Bartholomé and J. Karweil⁹ suggested free internal rotation in this molecule, but it is now certain that a considerable restricting potential exists. J. D. Kemp and K. S. Pitzer¹⁰ compared the measured and the calculated entropies and inferred a barrier of 3150 cal. per mol. The analysis of the vibrational spectra of ethane and hexadeuteroethane led F. Stitt¹¹ to a more precise assignment of the vibration frequencies, and a comparison of the measured and the calculated specific heats by G. B. Kistiakowsky, J. R. Lacher, and F. Stitt¹² then gave a value of 2750 cal. Confirmation of a value close to 3000 cal. is obtained from the statistical calculation of the ethylene-hydrogen-ethane equilibrium by E. A. Guggenheim.¹³ Neither the spectroscopic data nor a consideration of the symmetry number throws much light on whether the molecule is eclipsed or staggered, although for other reasons it now seems that the stable configuration is probably the staggered form. Both the entropy and the specific heat of dimethylacetylene show that in this molecule, by contrast, the restricting barrier is close to zero¹⁴ and certainly less than 500 cal. per mole. It might then be inferred that mere separation of the two methyl groups is a controlling factor in fixing the height of the barrier. Against this hypothesis, however, is the estimate by Stitt¹⁵ of 4000—6000 cal. for the barrier in diborane by a comparison of the measured and the calculated specific heats. The separation of the methyl groups in diborane is greater than in ethane. With neopentane, $C(CH_3)_4$, J. G. Aston, R. M. Kennedy, and G. H. Messerly¹⁶ estimate a barrier of about 4200 cal. restricting each methyl group, whereas in tetramethylsilicon¹⁷ it is about 1300 cal. These facts suggest that more subtle factors than mere separation of the rotating groups are operative, and there is a suggestion that a repulsive force may exist between the interacting centres which varies with a high power of the distance. Specific-heat data, together with the vibrational assignment of R. G. Owens and E. F. Barker,¹⁸ led J. G. Aston and P. M. Doty¹⁹ to a value of 1500 cal. for the barrier in methylamine, and J. G. Aston, M. L. Eidinoff, and W. S. Forster²⁰ similarly find a potential of 3460 cal. per methyl group in dimethylamine. Torsion of each methyl group in dimethyl sulphide²¹ appears to be impeded by a

⁹ *Z. physikal. Chem.*, 1938, **B**, **39**, 1. ¹⁰ *J. Amer. Chem. Soc.*, 1937, **59**, 276.

¹¹ *J. Chem. Physics*, 1939, **7**, 297.

¹² *Ibid.*, p. 289; see also G. B. Kistiakowsky and W. W. Rice, *ibid.*, pp. 281, 289.

¹³ *Trans. Faraday Soc.*, 1941, **37**, 97.

¹⁴ D. W. Osborne, C. S. Garner, and D. M. Yost, *J. Amer. Chem. Soc.*, 1941, **63**, 3492; *J. Chem. Physics*, 1940, **8**, 131; B. L. Crawford and W. W. Rice, *ibid.*, 1939, **7**, 437.

¹⁵ *Ibid.*, 1940, **8**, 981.

¹⁶ *J. Amer. Chem. Soc.*, 1936, **58**, 2354; 1937, **59**, 1743; see also K. S. Pitzer, *J. Chem. Physics*, 1937, **5**, 469, and J. G. Aston, *Chem. Reviews*, 1940, **27**, 59.

¹⁷ *J. Amer. Chem. Soc.*, 1940, **62**, 2567; 1941, **63**, 2343.

¹⁸ *J. Chem. Physics*, 1940, **8**, 229.

¹⁹ *Ibid.*, p. 637.

²⁰ *J. Amer. Chem. Soc.*, 1939, **61**, 1539.

²¹ D. W. Osborne, R. N. Doescher, and D. M. Yost, *J. Chem. Physics*, 1940, **8**, 506; H. W. Thompson, *Trans. Faraday Soc.*, 1941, **37**, 38.

potential of about 2000 cal.; for dimethyl ether²² R. M. Kennedy, M. Sagenkahn, and J. G. Aston find 3100 cal. and G. B. Kistiakowsky and W. W. Rice²³ 2500 cal. per methyl group. Rotation about the C-O bond has been considered in methyl alcohol, where a comparison of the observed and the calculated entropy²⁴ suggests a barrier of 3400 cal. per mole; this seems more probable than a lower value suggested by J. S. Koehler and D. M. Dennison.²⁵ In the same way from the calorimetric entropy and the vibrational frequency assignment of methylthiol, D. M. Yost²⁶ estimates a barrier of about 2000 cal. in this molecule for torsion about the C-S bond. In the case of allene, Kistiakowsky and Rice²⁷ have found close agreement between the calculated and the measured specific heats, verifying the belief that the potential barrier preventing rotation about a double bond is very high. Various estimates of the barrier in propylene have been made, by Pitzer,²⁸ by Kistiakowsky, J. R. Lacher, and W. W. Ransom,²⁹ by Kistiakowsky, B. L. Crawford, W. W. Rice, A. J. Wells, and E. B. Wilson,³⁰ and by D. Telfair and W. H. Pielemeier.³¹ Whereas Pitzer suggests 800 cal., Kistiakowsky and his colleagues find a value of 2100 cal. The disagreement arises primarily from differences in the vibrational assignment which was assumed, but the higher value has now been confirmed by the more extended study of the specific heat at higher temperatures by Telfair and Pielemeier. K. S. Pitzer has measured the variation of the specific heat of nitromethane³² over a wide range of temperature and has estimated the entropy; the vibrational spectrum has been measured by A. J. Wells and E. B. Wilson,³³ and a comparison gives a torsional barrier of about 800 cal. per mole. In acetaldehyde³⁴ the barrier appears to be considerable and of the order 2000 cal.

Less certain data are available for a series of other molecules such as acetone and isopropyl alcohol. These have been collected and discussed by Pitzer, Aston, Wilson, and Parks in an important symposium on chemical thermodynamics.³⁵ The evaluation of the thermodynamic properties of hydrocarbons in general is of particular importance in connexion with the possible occurrence of many industrial processes relating to the production of fuels. Some of these properties have been measured, *e.g.*, for butane, isobutane, pentane, heptane, and certain isohexanes and isooctanes.³⁶ Pitzer has now tried to formulate general expressions³⁷ for calculating these properties for long-chain normal or *iso*-hydrocarbons, assuming a constant value for the restricting barrier potential of similar adjacent groupings in all

²² *J. Amer. Chem. Soc.*, 1941, **63**, 2267.

²⁴ B. L. Crawford, *ibid.*, p. 744.

²⁶ D. M. Yost, private communication.

²⁸ *Ibid.*, 1937, **5**, 473.

³⁰ *J. Amer. Chem. Soc.*, 1939, **61**, 2980.

³² *J. Amer. Chem. Soc.*, 1941, **63**, 3313.

³⁴ H. W. Thompson and G. P. Harris, *Trans. Faraday Soc.*, in the press.

³⁵ *Chem. Reviews*, 1940, **27**, 1-85.

³⁶ See K. S. Pitzer *et al.*, *J. Amer. Chem. Soc.*, 1940, **62**, 1917, 1224, 2988; 1941, **63**, 2413; *J. Chem. Physics*, 1940, **8**, 711; *Chem. Reviews*, 1940, **27**, 39.

³⁷ *J. Chem. Physics*, 1940, **8**, 711; *Chem. Reviews*, 1940, **27**, 39.

²³ *J. Chem. Physics*, 1940, **8**, 610, 618.

²⁵ *Physical Rev.*, 1940, **57**, 1006.

²⁷ *J. Chem. Physics*, 1940, **8**, 610, 618.

²⁹ *Ibid.*, 1938, **6**, 900.

³¹ *J. Chem. Physics*, 1941, **9**, 571.

³³ *J. Chem. Physics*, 1941, **9**, 314.

cases. The usefulness of such a treatment, though as yet necessarily approximate, is already apparent, and it is to be expected that refinements will shortly follow.

Reference should also be made to earlier measurements of the entropy of dinitrogen tetroxide by W. F. Giaque and J. D. Kemp;³⁸ the vibrational frequency assignment of this molecule is still somewhat uncertain, but the data appear definitely to suggest a fairly high potential preventing the two NO₂ end groups from rotating with respect to each other. In an attempt to estimate the barrier in ethyl chloride, J. W. Linnett³⁹ has compared the measured equilibrium constants of the reaction ethylene-hydrogen chloride-ethyl chloride with those calculated on the assumption of different barrier heights. Unfortunately here, as in many other cases, the experimental data on the equilibrium constants do not seem sufficiently accurate for the purpose required.

The rotational structure of the infra-red absorption bands of a few lighter molecules provides semi-quantitative data about internal rotation. For the purpose of considering this rotational structure, molecules are usually classified according to their symmetry, since, in part, this determines the arrangement of the rotation lines. In reality, however, most molecules are asymmetrical rotators, having all three moments of inertia unequal, and the rotational structure in these cases is very complex. At the same time, some molecules approximate sufficiently closely to a symmetrical top ($I_A = I_B \neq I_C$) for the rotational structure of their vibration bands to deviate only slightly from that to be expected for the symmetrical rotator. The absorption bands may be of two types, according as the change in electric moment is parallel or perpendicular to the symmetry axis, and these respective rotational structures have been described in a recent Report.⁴⁰ For our present purpose the main point is that the structure of a perpendicular type band may be fundamentally affected by the occurrence of internal rotation. A theoretical treatment of the energy levels of a torsional oscillator was first given by A. H. Nielsen.⁴¹ Qualitatively the results may be expressed by saying that if there is free internal rotation the spacing between the *Q* branches of the perpendicular type bands is much increased above its value for the rigid molecule. The exact theoretical background of the phenomenon is not yet fully worked out, but the effect can conveniently be sought in the infra-red bands of such molecules as ethane, methyl alcohol, and methylamine. J. B. Howard⁴² first showed that the rotational structure of certain infra-red bands of ethane is consistent with a barrier of about 2000 cal. resisting rotation about the C-C bond. This value compares reasonably with the value given in the preceding paragraphs. The rotational structure of a harmonic band of the O-H bond vibration in methyl alcohol, photographed by R. M. Badger and S. H. Bauer,⁴³ is consistent with a fairly high restricting potential about this bond. The analysis of the absorption bands of this

³⁸ *J. Chem. Physics*, 1938, 6, 40.

⁴⁰ *Ann. Reports*, 1935, 32, 53.

⁴² *J. Chem. Physics*, 1937, 5, 451.

³⁹ *Trans. Faraday Soc.*, 1940, 36, 527.

⁴¹ *Physical Rev.*, 1932, 40, 445.

⁴³ *Ibid.*, 1936, 4, 469.

molecule at longer wave-lengths led A. Borden and E. F. Barker⁴⁴ to a value of about 1500 cal., which seems on other grounds to be too low. Their data have also been discussed by J. S. Koehler and D. M. Dennison.⁴⁵ The rotational analysis of a photographic infra-red band of methylamine by H. W. Thompson⁴⁶ shows that this molecule is essentially rigid. A. P. Cleaves, H. Spomer, and L. G. Bonner⁴⁷ agree with this conclusion, which accords with the thermodynamic-statistical considerations given above.

Many papers continue to appear dealing with the application of Raman spectral data to this problem. If rotational isomers exist, arising from an internal potential barrier resisting torsion, the number of Raman intervals for a given substance will be greater than might be expected for a single component, and by the application of selection rules and the measurement of polarisation properties it might, in theory, be possible to assign the different frequency intervals to characteristic vibrations of different symmetry types, such as eclipsed and staggered configurations. K. W. F. Kohlrausch⁴⁸ and his collaborators have examined a wide range of compounds in which torsion is possible, and claim definite conclusions in many cases. The majority prefer to think, however, that this method can rarely be unambiguous. W. F. Edgell and G. Glockler⁴⁹ have reviewed the whole position with particular reference to the alkyl halides and dihalogenoethanes. They point out that, although there seems to be clear evidence that the higher alkyl halides exist in two forms, the evidence as to their form—*cis*-, *trans*-, or otherwise—is far less conclusive. With the dihalogenoethanes the facts are thought to be in best agreement with the hypothesis that the two forms are the *trans*-form and the pair of identical C₂ staggered structures, the latter being obtained from the former by an internal rotation through 120°. Edgell and Glockler conclude that there is no evidence for a *cis*-(eclipsed) form of a molecule of the ethane type. G. Glockler and C. Sage⁵⁰ also believe that the staggered forms are predominant in a series of multihalogenated ethanes. Ta You Wu⁵¹ arrives at a different result, and A. Langseth, H. J. Bernstein, and B. Bak⁵² claim that Raman measurements on 2-bromo-1-deuteroethane show that the rotational isomers have the eclipsed (opposed) configurations, from which an eclipsed structure of ethane is inferred. Langseth and Bak⁵³ have extended their hypothesis of the stability of opposed structures to a consideration of the form of *cyclohexane*. The Raman data of this molecule and of deutero-substituted *cyclohexanes* are said to be consistent with a planar *cyclohexane* ring, with the hydrogen atoms in opposed positions with respect to neighbouring hydrogen atoms. Langseth and Bernstein⁵⁴ applied the hypothesis of opposed structures further in con-

⁴⁴ *J. Chem. Physics*, 1938, **6**, 553.

⁴⁵ *Physical Rev.*, 1940, **57**, 1006.

⁴⁶ *J. Chem. Physics*, 1938, **6**, 775; 1939, **7**, 448.

⁴⁷ *Ibid.*, 1940, **8**, 784.

⁴⁸ See a series of papers in *Z. physikal. Chem.*, especially 1940, *B*, **46**, 165; *B*, **47**, 65, 155; 1939, *B*, **45**, 329, 341; 1940, *B*, **48**, 1.

⁴⁹ *J. Chem. Physics*, 1941, **9**, 375.

⁵⁰ *Ibid.*, p. 375.

⁵¹ *Ibid.*, 1939, **7**, 965.

⁵² *Ibid.*, 1940, **8**, 430.

⁵³ *Ibid.*, p. 403.

⁵⁴ *Ibid.*, p. 410.

nexion with the Raman spectrum of tetrachloroethane and the effect of temperature upon it. That eclipsed structures, as proposed by Langseth and his colleagues, are unsatisfactory, has been pointed out by several authors. Many workers appear to overlook the fact that with liquids the selection rules for the Raman effect may cease to operate rigidly, because of distortions leading to alteration of the molecular symmetry. In particular, V. Schomaker and D. P. Stevenson⁵⁵ and K. S. Pitzer⁵⁶ have shown that evidence of different kinds strongly favours the staggered forms, and some form of repulsive interaction between neighbouring non-bonded atoms. Measurements on the heats of bromination of certain unsaturated cyclic hydrocarbons seem also to support this idea.⁵⁷

General Thermodynamics.—In addition to the examples referred to in the previous section, the thermodynamic properties of many other molecules have been computed from spectroscopically determined molecular magnitudes. In some cases the calculated values have been compared with direct measurements, and in nearly all cases a close agreement has been found. Thus, measured and calculated entropies have been compared for methyl chloride,⁵⁸ hydrogen cyanide,⁵⁹ cyanogen,⁶⁰ and arsenic trifluoride;⁶¹ and specific heats for ethylene,⁶² cyanogen,⁶³ and several lower hydrocarbons.⁶⁴ Certain equilibrium data have been used to compare calculated and measured free energies. This last method has been applied to check the frequency assignment in nitrosyl chloride,⁶⁵ to derive a more probable value for the heat of formation of carbonyl chloride,⁶⁶ and to show the desirability of a re-examination of the thermal dissociation of sulphuryl chloride.⁶⁷ D. Grafe, K. Clusius, and A. Kruis⁶⁸ obtain satisfactory agreement between the measured and the calculated equilibrium $D_2 + H_2S \rightleftharpoons D_2S + H_2$. A series of papers deals with the thermodynamic properties of hydrocarbons which are of particular importance in modern fuels.⁶⁹

Other calculated values are available for phosphorus,⁷⁰ phosphine, the

⁵⁵ *J. Chem. Physics*, 1940, **8**, 637.

⁵⁶ *J. Amer. Chem. Soc.*, 1941, **63**, 3313; see also J. G. Aston, S. G. Schumann, H. L. Fink, and P. M. Doty, *ibid.*, p. 2029.

⁵⁷ M. W. Lister, *ibid.*, p. 143; G. B. Kistiakowsky, *ibid.*, 1939, **61**, 1868.

⁵⁸ G. H. Messerly and J. G. Aston, *ibid.*, 1940, **62**, 887.

⁵⁹ R. A. Ruehrwein and W. F. Giauque, *ibid.*, 1939, **61**, 2626.

⁶⁰ *Idem*, *ibid.*, p. 2940.

⁶¹ H. Powell, R. F. Rundle, and D. M. Yost, *ibid.*, 1941, **63**, 2825.

⁶² E. J. Burcik, E. H. Eyster, and D. M. Yost, *J. Chem. Physics*, 1941, **9**, 118.

⁶³ E. J. Burcik and D. M. Yost, *ibid.*, 1939, **7**, 1114; F. Stitt, *ibid.*, p. 1115.

⁶⁴ J. G. Aston and G. H. Messerly, *J. Amer. Chem. Soc.*, 1940, **62**, 1917; J. G. Aston, R. M. Kennedy, and S. G. Schumann, *ibid.*, p. 2059; J. D. Kemp and C. J. Egan, *ibid.*, 1938, **60**, 1521.

⁶⁵ C. M. Beeson and D. M. Yost, *J. Chem. Physics*, 1939, **7**, 44.

⁶⁶ H. W. Thompson, *Trans. Faraday Soc.*, 1941, **37**, 251.

⁶⁷ *Idem*, *ibid.*, p. 340.

⁶⁸ *Z. physikal. Chem.*, 1939, **B**, **43**, 1.

⁶⁹ See *J. Amer. Chem. Soc.*, 1940, **62**, 1224, 1917, 2988; 1941, **63**, 1133, 2029, 2413; *J. Chem. Physics*, 1940, **8**, 711; *Chem. Reviews*, 1940, **27**, 39.

⁷⁰ D. P. Stevenson and D. M. Yost, *J. Chem. Physics*, 1941, **9**, 403.

phosphorus halides, several halogenomethanes,⁷¹ formaldehyde and deuterio-formaldehyde,⁷² diatomic hydrides and halides,⁷³ hydrazoic acid,⁷⁴ the cyanogen halides,⁷⁵ methyl cyanide⁷⁶ and isocyanide, hydrogen fluoride, fluorine,⁷⁷ and carbon suboxide.⁷⁸

The specific-heat measurements of G. B. Kistiakowsky and his collaborators in recent years have made it possible to correct previously measured heats of hydrogenation of unsaturated hydrocarbons to absolute zero and to the non-vibrating states of molecules.⁷⁹ As a result it is found that the heat change in a hydrogenation reaction definitely depends on the nature of the groups adjacent to the bonds being reduced, and it must be concluded that these contiguous groups appreciably influence the bonding strength of the unsaturated link. In a very interesting attempt to obtain a general formula for the entropy of long-chain compounds, M. L. Huggins⁸⁰ has used an approximate model to derive simple expressions for the contribution of the various degrees of freedom to this property, which agrees well with values so far measured for short-chain paraffins. The problem of the energy levels, partition function, and thermodynamic properties of molecules like ammonia with a double minimum potential energy function, has been considered by K. S. Pitzer,⁸¹ and by R. F. Haupt and E. Teller.⁸² Reference should also be made to a general symposium on thermodynamics,⁸³ where other references are compiled.

Concurrently with these developments in our knowledge of thermodynamic functions, further studies have been made of the best equations of state for vapours, and virial coefficients have been determined in some cases. The considerable progress made in developing a theory of liquids must be left over for a future report.

Infra-red and Raman Spectra.—Since about 1930 valuable and highly accurate data about molecular structure have been obtained from the study of the absorption bands of the vapours of some simpler polyatomic molecules in the photographic region of the infra-red, *viz.*, between 0.7 and 1.2 μ (7000 and 12,000 Å.). The success of this method lies in the ease with which high resolving power can be obtained by means of an ordinary diffraction grating. It was clear from the start, however, that this region would have limited applicability, since in order to bring the absorption into this spectral range, several vibrational quanta must be absorbed simultaneously, and the path

⁷¹ W. F. Edgell and G. Glockler, *J. Chem. Physics*, 1941, **9**, 484; D. W. Osborne, C. S. Garner, R. N. Doescher, and D. M. Yost, *J. Amer. Chem. Soc.*, 1941, **63**, 3496.

⁷² H. W. Thompson, *Trans. Faraday Soc.*, 1941, **37**, 251.

⁷³ D. P. Stevenson, *J. Chem. Physics*, 1941, **9**, 898.

⁷⁴ E. H. Eyster and R. H. Gillette, *ibid.*, 1940, **8**, 369.

⁷⁵ D. P. Stevenson, *ibid.*, p. 171.

⁷⁶ R. H. Ewell and J. F. Bourland, *ibid.*, p. 365.

⁷⁷ G. M. Murphy and J. E. Vance, *ibid.*, 1939, **7**, 806.

⁷⁸ H. W. Thompson, *Trans. Faraday Soc.*, 1940, **37**, 249.

⁷⁹ G. B. Kistiakowsky, J. B. Lachor, and R. W. Ransom, *J. Chem. Physics*, 1940, **8**, 970.

⁸⁰ *Ibid.*, p. 181.

⁸¹ *Ibid.*, p. 925.

⁸² *Ibid.*, 1939, **7**, 251.

⁸³ *Chem. Reviews*, 1940, **27**, 1—85.

length of vapour required increases very rapidly for each successive harmonic. Thus even with compounds containing a C-H bond of relatively high vibration frequency, three or four will be required, and for heavier molecules many more. In the case of heavier molecules, too, the larger moments of inertia will preclude the resolution of fine structure. Hence, the usefulness of this spectral region appears now to have been exhausted, so far at least as resolution of the rotational structure of bands is concerned. It is therefore opportune to review some of the most recent investigations in this field.

Perhaps the most striking of these is the measurement by L. Zumwalt and P. A. Giguère⁸⁴ of the absorption of the second overtone of the O-H bond vibration in hydrogen peroxide vapour at 0.97μ . The rotational structure found for this band is of particular importance, since it appears to settle finally the question as to whether the molecule has a planar or a non-planar structure. In principle, the OH groups of hydrogen peroxide may be either in the *cis*- or the *trans*-position with respect to each other, or in some intermediate non-planar position. If the molecule is non-planar, the hindering potential towards internal rotation will have two minima of equal depth and two barriers of unequal height, and there will be two enantiomorphic forms. According to the height of the potential barrier, there will be free rotation, restricted rotation, or a torsional oscillation. If the molecule had a *cis*-structure, the change in electric moment accompanying the O-H link vibration would be either entirely parallel or entirely perpendicular to the symmetry axis. The band observed appears, in fact, to be double and to have a peculiar hybrid structure, with features characteristic of both the parallel and the perpendicular band types, thus implying that the structure is not *cis*-. The large dipole moment measured by E. P. Linton and O. Maass⁸⁵ shows, on the other hand, that it is not *trans*-. A non-planar structure is therefore the only alternative. At the same time the finer details of the rotational structure of the infra-red band show that the molecule is not quite a symmetrical rotator, as it would be if the azimuthal angle between the directions of the two O-H bonds were 90° , since then two of the moments of inertia would be equal. An azimuthal angle of about 106° is suggested, so that the O-H bonds are set obliquely to each other. These conclusions are especially interesting in view of the earlier considerations of G. B. B. M. Sutherland and W. G. Penney.⁸⁶

E. H. Eyster⁸⁷ has measured the third and fourth harmonics of the N-H stretching vibration in hydrazoic acid vapour, and the rotational structure of the bands shows that the molecule is not completely linear, as has been suggested by some investigators. The bond lengths calculated are N-H, 1.012 \AA ; $\text{N}_1\text{-N}_2$, 1.241 \AA ; $\text{N}_2\text{-N}_3$, 1.128 \AA ; and the angle HNN is $110^\circ 52'$. Bands of methylamine vapour have been photographed by H. W. Thompson,⁸⁸ one only showing resolved rotational structure charac-

⁸⁴ *J. Chem. Physics*, 1941, **9**, 458.

⁸⁶ *J. Chem. Physics*, 1934, **2**, 492.

⁸⁸ *Ibid.*, 1939, **7**, 448.

⁸⁵ *Canadian J. Res.*, 1932, **5**, 81.

⁸⁷ *Ibid.*, 1940, **8**, 135, 369.

teristic of the perpendicular type vibration of a slightly asymmetrical rotator, and the rotational analysis gives results which agree with the molecular structural constants to be expected on other grounds, *viz.*, C-N, 1.47 Å.; N-H, 1.02 Å.; and CNH angle of 108° with a tetrahedral methyl group. This result has been confirmed by A.P. Cleaves, H. Spomer, and L. G. Bonner,⁸⁹ who also measured bands of dimethylamine.

After much discussion the structure of ethylene appears now to have been fixed by the measurement of two bands⁹⁰ in the region of 1μ, one being essentially parallel type, and the other perpendicular. Values for all the moments of inertia have been deduced, and the C-H bond length being assumed to be 1.085 Å., it is found that the carbon-carbon bond length is 1.331 Å. and the angle HCH 118°. These values have been confirmed by a completely independent measurement of some infra-red bands by L. G. Smith.⁹¹

The fourth harmonic of the O-H vibration in formic acid vapour, measured by H. W. Thompson,⁹² has a hybrid structure in which the perpendicular component is very marked, similar to that of the third harmonic previously photographed by R. M. Badger and S. H. Bauer.⁹³ Although exact figures for the molecular dimensions cannot be obtained, the structure of these bands gives a qualitative picture of the form of the molecule. Similar qualitative information is obtained from the structure of a band of formaldehyde vapour measured by L. Zumwalt and R. M. Badger.⁹⁴ H. W. Thompson⁹⁵ has surveyed the absorption between 0.7 and 1.2μ of a residuum of molecules thought likely to have bands with resolvable rotational structure.

W. H. J. Childs and H. A. Jahn⁹⁶ have measured the spectrum of deuteromethane in the photographic infra-red. A band at 1.1μ has a simple structure, which leads to a C-H bond length of 1.093 Å. These authors have also discussed some complexities in certain bands of methane, one of which is of theoretical significance for all molecules having a three-fold or higher axis of symmetry. Interesting features of the absorption by pyrrole vapour at about 1μ have been noted by Zumwalt and Badger.⁹⁷

Recent infra-red work at longer wave-lengths covers a wide field, and it is not possible to refer to all the subjects studied by measurement of the molecular absorption spectra in this region. The importance of the method as a means of analysis is now being fully realised.⁹⁸ As a means of simplifying vibrational analysis and the assignment of frequencies to particular normal modes, the spectra of molecules and their deuterium analogues have been employed. In this way F. Stitt⁹⁹ has established the normal vibrational

⁸⁹ *J. Chem. Physics*, 1940, **8**, 784.

⁹⁰ H. W. Thompson, *Trans. Faraday Soc.*, 1939, **35**, 697.

⁹¹ *J. Chem. Physics*, 1941, **8**, 798.

⁹² *Ibid.*, 1936, **4**, 469.

⁹³ *Ibid.*, 1939, **7**, 235.

⁹⁴ *Ibid.*, 1939, **7**, 453.

⁹⁵ *Ibid.*, p. 441.

⁹⁶ *Proc. Roy. Soc.*, 1939, **A**, **169**, 428, 451; **A**, **171**, 450.

⁹⁷ *J. Chem. Physics*, 1939, **7**, 629.

⁹⁸ See, *e.g.*, N. Wright, *Ind. Eng. Chem. (Anal.)*, 1941, **13**, 1; W. H. Avery, *J. Opt. Soc. Amer.*, 1941, **31**, 633.

⁹⁹ *J. Chem. Physics*, 1939, **7**, 297.

frequencies of ethane and hexadeuteroethane, and of acetylene and the deuterioacetylenes.¹ G. K. T. Conn and G. B. B. M. Sutherland² have similarly studied tetradeuteroethylene and have cleared up some doubtful points connected with the vibrations of ethylene. E. Lee and C. K. Wu³ have analysed the rotational structure of some vibration bands of arsine, trideuteroarsine, and trideuterophosphine, and from the resulting data Sutherland, Lee, and Wu⁴ have estimated the dimensions of the molecular pyramid in each case. In phosphine the barrier restricting the passage of the phosphorus atom through the plane of the hydrogen atoms is about 2000 cm.^{-1} (about 6 kg.-cals.), a value close to that previously suggested for ammonia by D. M. Dennison and G. E. Uhlenbeck.⁵ Calculations suggest, however, that in the case of phosphine the substitution of large massive groups in place of the hydrogen atoms may give a molecule for which the frequency of inversion is small enough to permit the separation of optically active isomers at sufficiently low temperatures. A study of the spectra of hydrogen selenide, deuterium selenide, and deuterium hydrogen selenide by D. M. Cameron, W. C. Sears, and H. H. Nielsen⁶ has suggested a triangular structure for these molecules with an apex angle somewhat greater than a right angle. In this work the correctness of the vibrational assignment was checked by use of the product rules of O. Redlich.⁷ Structure of methyl chloride infra-red bands has been used to re-determine the C-Cl bond length.⁸

High resolving power has also been used in measuring the infra-red bands of other molecules. C. K. Wu and E. F. Barker⁹ partially resolved the rotational structure of several absorption bands of propane, and R. G. Owens and E. F. Barker¹⁰ obtained similar data for methylamine. The spectrum of the latter has been measured with lower resolution by C. R. Bailey, S. C. Carson, and E. F. Daly,¹¹ and by A. P. Cleaves and E. K. Plyler,¹² but a satisfactory vibrational analysis was achieved only with the help of the rotational fine structure found by Owens and Barker.¹³ D. H. Gage and E. F. Barker¹⁴ measured the vibrational spectrum of boron trifluoride and partially resolved certain bands. An estimated moment of inertia gives 1.29 Å. for the B-F distance, but a considerable vibrational-rotational interaction complicates the structure of some of the bands of this substance. The general problem of interaction between vibrational and rotational energy of polyatomic molecules has been examined by H. H. Nielsen, by S. Silver, W. H. Shaffer, and by Shaffer,¹⁵ and relevant effects in two parallel bands of

¹ *J. Chem. Physics*, 1940, **8**, 56.

² *Proc. Roy. Soc.*, 1939, **A**, **172**, 172.

³ *Trans. Faraday Soc.*, 1939, **35**, 1366.

⁴ *Ibid.*, p. 1373.

⁵ *Physical Rev.*, 1932, **41**, 313.

⁶ *J. Chem. Physics*, 1939, **7**, 994.

⁷ *Z. physikal. Chem.*, 1935, **B**, **28**, 371; *J. Chem. Physics*, 1937, **5**, 529.

⁸ G. B. B. M. Sutherland, *ibid.*, 1939, **7**, 1066.

⁹ *Ibid.*, 1941, **9**, 487.

¹⁰ *Ibid.*, 1940, **8**, 229.

¹¹ *Proc. Roy. Soc.*, 1940, **A**, **173**, 339.

¹² *J. Chem. Physics*, 1939, **7**, 563.

¹³ *Loc. cit.*, ref. (10).

¹⁴ *J. Chem. Physics*, 1939, **7**, 455.

¹⁵ H. H. Nielsen, *Physical Rev.*, 1941, **60**, 794; S. Silver and W. H. Shaffer, *J. Chem. Physics*, 1941, **9**, 599; W. H. Shaffer, *ibid.*, p. 607.

ammonia have been described by H. Y. Sheng, E. F. Barker, and D. M. Dennison.¹⁶ A. H. Nielsen measured rotational structure in some bands of deuterioacetylene,¹⁷ and H. H. Nielsen has re-examined certain absorption bands of water vapour.¹⁸ L. G. Smith¹⁹ used the rotational structure of a parallel type band of ethylene to deduce the moments of inertia, as referred to above. A Coriolis perturbation similar to that discussed by W. H. J. Childs and H. A. Jahn for methane bands has been observed and measured by G. M. Murphy²⁰ in the spectra of silane and germane.

Some molecules which have been studied in order to determine the fundamental vibration frequencies include cyanogen,²¹ nitromethane,²² propylene,²³ methylacetylene,²⁴ and dimethylacetylene.²⁵ Absorption bands of hydrazoic acid vapour have been measured by M. M. Davies,²⁶ and by Eyster,²⁷ who also examined methyl azide and methyl isocyanate. The spectrum of hydrazine has been recorded by W. Fresenius and J. Karweil.²⁸ The vibration frequencies of ethylene sulphide have been determined by H. W. Thompson and D. J. Dupré,²⁹ of dimethyl sulphide by R. Fonteyne³⁰ and by H. W. Thompson,³¹ and of methylthiol by H. W. Thompson and N. P. Skerrett.³² Other molecules investigated in this connexion include dimethyl ether,³³ dimethylzinc,³⁴ ethyleneimine,³⁵ acetaldehyde,³⁶ and several hydrocarbons such as *n*-pentane.³⁷

J. J. Fox and A. E. Martin³⁸ have examined the variation in the characteristic vibration bands of the C-H bond in the region of 3μ in a series of paraffins and olefins. The characteristic frequencies of this bond differ slightly according to the precise group of which it forms a part, but they seem to remain reasonably constant for a given type of C-H bond in a large series of molecules. Similarly, in α - and β -methylnaphthalenes, quinoline and isoquinoline, and similar molecules, small differences are traced in the region of absorption of C-H bond vibrations which appear to provide a basis for the analysis of these compounds.³⁹ Infra-red studies on the proteins and related substances continue,⁴⁰ and the effect of state of aggregation upon

¹⁶ *Physical Rev.*, 1941, **60**, 786.

¹⁷ *Ibid.*, 1940, **57**, 346.

¹⁸ *Ibid.*, 1940, **59**, 565.

¹⁹ *J. Chem. Physics*, 1941, **9**, 798.

²⁰ *Ibid.*, 1940, **8**, 71.

²¹ *Ibid.*, 1939, **7**, 859.

²² A. J. Wells and E. B. Wilson, *ibid.*, 1941, **9**, 314.

²³ E. B. Wilson and A. J. Wells, *ibid.*, p. 319.

²⁴ B. L. Crawford, *ibid.*, 1939, **7**, 140; 1940, **8**, 526.

²⁵ *Idem*, *ibid.*, 1939, **7**, 553.

²⁶ *Trans. Faraday Soc.*, 1939, **35**, 1184.

²⁷ *J. Chem. Physics*, 1940, **8**, 369.

²⁸ *Z. physikal. Chem.*, 1940, **B**, **44**, 1.

²⁹ *Trans. Faraday Soc.*, 1940, **36**, 805.

³⁰ *J. Chem. Physics*, 1940, **8**, 60.

³¹ *Trans. Faraday Soc.*, 1941, **37**, 38.

³² *Ibid.*, 1940, **36**, 812.

³³ B. L. Crawford and L. Joyce, *J. Chem. Physics*, 1939, **7**, 307.

³⁴ H. W. Thompson, J. W. Linnett, and F. J. Wagstaffe, *Trans. Faraday Soc.*, 1940, **36**, 797.

³⁵ H. W. Thompson and W. G. Leeds, *ibid.*, in the press.

³⁶ H. W. Thompson and G. P. Harris, *ibid.*, in the press.

³⁷ G. C. Stinchcomb, *J. Chem. Physics*, 1939, **7**, 853.

³⁸ *Proc. Roy. Soc.*, 1939, **A**, **175**, 208.

³⁹ *J.*, 1939, 318.

⁴⁰ J. W. Bath and J. Ellis, *J. Physical Chem.*, 1941, **45**, 204; A. M. Buswell, K. F. Krebs, and W. H. Rodebush, *J. Chem. Physics*, 1940, **8**, 1126.

infra-red absorption bands has been examined.⁴¹ Fox and Martin⁴² have measured the spectra of both liquid water and ice and discussed their results in relation to the structure of liquid water. On the theoretical side reference must be made to a further article by D. M. Dennison on the infra-red spectra of polyatomic molecules.⁴³

Of the many measurements of Raman spectra recently made, only a few can be mentioned here. Apparatus is described by J. S. Kirby-Smith and L. G. Bonner⁴⁴ for obtaining the Raman displacements with gases, using reasonable exposure times, and these authors have first studied methylamine vapour. The fine structure of Raman lines of carbon tetrachloride has been measured by A. C. Menzies,⁴⁵ and found to be consistent with an explanation in terms of chlorine isotopy, and also with the abundance ratio to be expected. The carbon isotope shifts have been calculated for a series of acetylenic compounds by F. F. Cleveland and M. T. Murray,⁴⁶ and compared with experimental data.

A particularly interesting series of Raman measurements has been carried out by G. Glockler⁴⁷ and his collaborators for the halogenated methanes. The alteration in the observed displacements as the substituents are changed one by one is valuable in assigning the magnitudes to different vibrational modes, and these data should prove valuable for the calculation of force constants and force fields for this type of molecule. Another series of molecules whose Raman spectra have proved interesting is a group of metallic and non-metallic alkyls.⁴⁸ The displacements observed with octane, decane, and higher hydrocarbons are complex and not easily interpreted.⁴⁹

Potential Energy Functions, Force Constants, and General Structural Relationships.—The importance of force constants as a measure of the nature and strengths of linkages has been referred to in previous Reports, in which the principles underlying these calculations and the approximations necessary have been explained.⁵⁰ Serious discrepancies were noticed, however, in some of the earlier computations by different workers for the same molecules. It is clear that the exact significance of the magnitudes described as force constants depends upon the particular potential energy function used to describe the molecular vibrations. Several types of function have from time to time been adopted, the most common being that which assumes forces consistent with the idea of conventional valency bonds, and known as valency force field. Internal molecular interactions, however, which are

⁴¹ See, e.g., W. West, *J. Chem. Physics*, 1939, 7, 795; G. B. B. M. Sutherland *et al.*, *Proc. Roy. Soc.*, 1941, A, 176, 484, 493.

⁴² *Ibid.*, 1940, A, 174, 234.

⁴³ *Rev. Mod. Physics*, 1940, 12, 175; 1931, 3, 280.

⁴⁴ *J. Chem. Physics*, 1939, 7, 880.

⁴⁵ *Proc. Roy. Soc.*, 1939, A, 172, 89.

⁴⁶ *J. Chem. Physics*, 1941, 9, 390.

⁴⁷ G. Glockler and G. R. Leader, *ibid.*, 1940, 8, 125, 699; G. Glockler and C. Sage, *ibid.*, p. 291; J. Kahovec and J. Wagner, *Z. physikal. Chem.*, 1940, B, 47, 48; B, 48, 188.

⁴⁸ E. J. Rosenbaum, D. J. Rubin, and C. R. Sandberg, *J. Chem. Physics*, 1940, 8, 366.

⁴⁹ E. J. Rosenbaum, *ibid.*, 1941, 9, 295.

⁵⁰ *Ann. Reports*, 1936, 33, 59.

to a large extent specific, make this simple type of force field seldom rigidly applicable, although in some cases an apparently satisfactory solution is obtained, perhaps by a fortuitous cancellation of a series of inaccuracies. It is customary to find that a simple potential function of this type fails to account satisfactorily for the entire array of frequencies of a molecule. More complex functions must therefore be assumed, and tested by their individual performance. In some cases the number of "constants" which have to be introduced in order to obtain a complete prediction of all vibration frequencies for a given molecule may exceed the actual number of these frequencies. In such cases the reverse procedure of estimating the "constants" from the measured frequencies is usually not possible, unless additional vibration frequencies of an isotopic molecule which has the same potential function are available. It has been suggested, in fact, that the correctness of a given potential function may be measured by its ability to reproduce, not only the vibration frequencies of the molecule to which it applies, but also those of an isotopic molecule of the same composition.

This use of the isotope effect is particularly applicable to structures in which hydrogen may be replaced by deuterium, and several cases of this kind have now been examined. For example, F. Stitt obtained a self-consistent potential energy function for ethane and hexadeuteroethane,⁵¹ which accounts very well for all the fundamentals of these molecules. Stitt also studied acetylene and the deuterioacetylenes in the same way. Measurement of some of the infra-red bands of tetradeuteroethylene enabled G. K. T. Conn and G. B. B. M. Sutherland⁵² to compare the relative merits of different potential functions which have been proposed for ethylene.

It cannot be denied that the above method is a powerful one, but the number of molecules to which it can be applied in practice is small, since isotopic frequency changes are in general too small to be easily determinable. Another approach which has seemed attractive is to add to the conventional potential functions of simple valency force field such interaction terms as seem likely to be significant in the particular case, and to consider whether in a series of related molecules force constants can be carried over from one molecule to the next and predict its vibration frequencies correctly. This method was used some years ago by H. W. Thompson and J. W. Linnett⁵³ and has since been adopted with success by several authors. In this way Linnett⁵⁴ calculated the force constants of bonds in ethane, the methyl halides, methyl cyanide and isocyanide, and concluded that in methyl cyanide the carbon-carbon bond has some double-bond character, as suggested on other grounds by L. Pauling, H. D. Springall, and K. J. Palmer.⁵⁵ Interesting variations in the bending constants were also noted by Linnett. Z. I. Slawsky and D. M. Dennison's treatment⁵⁶ of the same molecules does not appear to be so satisfactory. B. L. Crawford and S. R. Brinckley⁵⁷ have also given a

⁵¹ *J. Chem. Physics*, 1939, 7, 297; 1940, 8, 56.

⁵² *Proc. Roy. Soc.*, 1939, A, 172, 172.

⁵³ *J. Chem. Physics*, 1940, 8, 91.

⁵⁴ *J. Chem. Physics*, 1939, 7, 522.

⁵⁵ *J.*, 1937, 1376.

⁵⁶ *J. Amer. Chem. Soc.*, 1939, 61, 927.

⁵⁷ *Ibid.*, 1941, 9, 69.

normal co-ordinate treatment of hydrogen cyanide, methyl cyanide, and the methyl halides which is closely similar to that of Linnett. They are able to calculate satisfactorily 52 vibration frequencies of this series of molecules from potential functions involving only 20 constants, and the main stretching constants of the bonds can be carried over from one molecule for use with the next. In a later paper, Linnett⁵⁸ has shown, however, that Crawford and Brinckley have used a carbon-carbon bond force constant which is probably in error, and has discussed a simple potential function not only for use with the methyl halides but also for methyl- and dimethyl-acetylene, which were previously treated by Crawford.⁵⁹ Ta You Wu⁶⁰ has also considered the potential function of acetylene, and it is perhaps relevant here to refer to an important paper by E. C. Baughan, M. G. Evans, and M. Polanyi⁶¹ on the nature of carbon-carbon linkages.

Other normal co-ordinate treatments have been carried out by S. Silver⁶² for structures of the type $M(\text{CH}_3)_4$, by E. J. Rosenbaum, D. J. Rubin, and C. R. Sandberg⁶³ for trimethyl-phosphine and -arsine (and by J. Wagner⁶⁴ for the methylene halides); and S. E. Whitcomb, H. H. Nielsen, and L. H. Thomas⁶⁵ have analysed the vibrations of a normal hydrocarbon chain with particular reference to undecane. L. Kellner⁶⁶ has carried through an extensive calculation on the force constants of links in urea and the guanidonium ion, but in a case of this kind it is doubtful whether the simple treatment used can be of much value, particularly in view of the uncertain experimental data.

The technique of the calculations involved in determining force constants has been further examined by E. B. Wilson, and simpler methods of dealing with the complex secular equations usually encountered have been suggested by B. Hicks.⁶⁷ J. O. Hirschfelder⁶⁸ has provided a compact formula by which the moments of inertia of irregular structures may be rapidly calculated. O. Redlich⁶⁹ studied the effect of vibrational anharmonicity on the potential function of polyatomic molecules.

All the above remarks imply the importance for chemical theory of knowing the potential functions of polyatomic molecules. Meanwhile a completely satisfactory general expression for the variation of potential energy of a diatomic molecule with internuclear separation is not yet known. The limitations of using the Morse equation for nuclear separations far removed from the stable position have been realised for some time, and efforts to obtain a better relationship have been made by H. M. Hulbert and J. O.

⁵⁸ *Trans. Faraday Soc.*, 1941, **37**, 469.

⁵⁹ *J. Chem. Physics*, 1939, **7**, 140, 553; 1940, **8**, 526.

⁶⁰ *Ibid.*, 1939, **7**, 178; 1940, **8**, 489.

⁶¹ *Trans. Faraday Soc.*, 1941, **37**, 377.

⁶² *J. Chem. Physics*, 1941, **8**, 919.

⁶³ *Ibid.*, 1940, **8**, 366.

⁶⁴ *Z. physikal. Chem.*, 1939, **B**, **45**, 69.

⁶⁵ *J. Chem. Physics*, 1940, **8**, 143.

⁶⁶ *Proc. Roy. Soc.*, 1941, **A**, **177**, 447, 456.

⁶⁷ E. B. Wilson, *J. Chem. Physics*, 1941, **9**, 76; 1939, **7**, 1047; B. Hicks, *ibid.*, 1940, **8**, 569.

⁶⁸ *Ibid.*, p. 431.

⁶⁹ *Ibid.*, 1941, **9**, 298.

Hirschfelder ⁷⁰ and by J. W. Linnett. ⁷¹ The last-named has examined the usefulness of a "reciprocal-exponential" function $U = ar^{-m} - be^{-nr}$, which incorporates features of both the standard Morse equation and the general double reciprocal formula $U = ar^{-m} - br^{-n}$. G. B. B. M. Sutherland ⁷² has recently used the double reciprocal function in attempting a derivation of the relation between force constant and equilibrium nuclear separation. Linnett has drawn attention to the shortcomings in Sutherland's treatment, and provides evidence on a wide variety of diatomic molecules to show that the reciprocal-exponential function is an improvement on other existing relationships. Incidentally, there is some indication that the relationship between force constant and nuclear separation $k_e r_e^6 = \text{const.}$, originally proposed by C. H. D. Clark, is more satisfactory than the Badger equation $(r_e - d_{ij})^3 = C_{ij}/k_e$, which has been found so useful in much recent work. In a further series of papers, Clark ⁷³ has developed his formulæ further and compared the relative merits of the various relationships.

J. J. Fox and A. E. Martin ⁷⁴ have also directed attention to some interesting relationships between force constant, bond length, and energy of some carbon-carbon bonds. A typical instance of the use of these semi-empirical relationships is found in the use by D. P. Stevenson ⁷⁵ of Badger's rule to determine the P-H bond length in phosphine (1.40 Å.) which, taken with the single moment of inertia obtained from the spectrum, leads to a value of the apex bond angles close to 93°. Stevenson also considered the structure of other hydrides. The connexion between bond length and bond strength has also been discussed by R. F. Barrow, ⁷⁶ D. Wrinch and D. Harker, ⁷⁷ M. Burton, ⁷⁸ and C. A. Coulson. ⁷⁹

Miscellaneous Spectroscopy.—Recent developments in ultra-violet spectroscopy include diverse topics, but these must be reserved for a future Report. Attention may be directed, however, to a review by H. Sponer and E. Teller ⁸⁰ on the ultra-violet spectra of polyatomic molecules, and some progress has been made in analysing the rotational structure of some of the bands. N. Metropolis ⁸¹ has considered the relevant theory for this rotational structure, which has been analysed for bands of sulphur dioxide and carbon disulphide. ⁸² Spectroscopy in the far ultra-violet is described by J. C. Boyce, ⁸³ and the rôle of optical measurements in the borderland of physical chemistry and biology has been outlined by J. R. Loofbourow. ⁸⁴

The Hydrogen Bond.—Progress in this subject has been reviewed fully in a recent discussion. ⁸⁵ In this, W. T. Astbury has outlined the evidence

⁷⁰ *J. Chem. Physics*, 1941, **9**, 61.

⁷¹ *Trans. Faraday Soc.*, 1940, **36**, 1123.

⁷² *J. Chem. Physics*, 1940, **8**, 161.

⁷³ *Trans. Faraday Soc.*, 1940, **36**, 370; 1941, **37**, 293, 299.

⁷⁴ *J.*, 1939, 884.

⁷⁵ *J. Chem. Physics*, 1940, **8**, 285.

⁷⁶ *Trans. Faraday Soc.*, 1940, **36**, 624, 1053.

⁷⁷ *J. Chem. Physics*, 1940, **8**, 502.

⁷⁸ *Ibid.*, p. 743.

⁷⁹ *Ibid.*, 1939, **7**, 1069.

⁸⁰ *Rev. Mod. Physics*, 1941, **13**, 75.

⁸¹ *Physical Rev.*, 1941, **60**, 283.

⁸² *Ibid.*, pp. 295, 496.

⁸³ *Rev. Mod. Physics*, 1941, **13**, 1.

⁸⁴ *Ibid.*, 1940, **12**, 272.

⁸⁵ *Trans. Faraday Soc.*, 1940, **36**, 871—928.

for the existence of hydrogen bridges in proteins, and C. E. H. Bawn, E. L. Hirst, and E. T. Young have concluded that some properties of starch are consistent with the union of macromolecules with each other through this type of link to form particles. G. B. B. M. Sutherland has summarised the application of infra-red spectroscopy to the problem, and J. J. Fox and A. E. Martin from a similar standpoint have given data on the specific cases of association of alcohols, and carboxylic acids, and internally chelated molecules. In the same symposium, J. M. Robertson has discussed the X-ray evidence for hydrogen bonds, and W. R. Angus and W. K. Hill have described preliminary work on diamagnetic susceptibilities (see this vol., p. 29) which appear to be capable of revealing the occurrence of this phenomenon.

Models for proteins involving hydrogen bonds have also been considered by M. L. Huggins,⁸⁶ and a series of papers deal with the associating properties of different solvents.⁸⁷ The infra-red association bands of several hydroxy-compounds in solution and in the solid state have been examined by M. M. Davies,⁸⁸ and polymerisation of hydrogen fluoride has been measured by A. Wahrhaftig⁸⁹ and by A. M. Buswell, R. L. Maycock, and W. H. Rodebush.⁹⁰ R. Mecke and his co-workers⁹¹ have developed a new technique for studying the association bands of alcohols in the photographic infra-red and have made calculations on the equilibrium relationships of the association. A consideration of boiling points and other physical properties, such as solubility in donor solvents, of a variety of pyrazole and indazole derivatives containing the imino-group has led to the suggestion that there is a bond of the type N—H—N in these molecules.⁹²

H. W. T.

W. R. ANGUS.

H. W. MELVILLE.

R. A. MORTON.

H. W. THOMPSON.

⁸⁶ *J. Chem. Physics*, 1940, **8**, 598.

⁸⁷ See, e.g., W. Gordy *et al.*, *J. Chem. Physics*, 1939, **7**, 93, 99, 163, 167; 1940, **8**, 170, 516; 1941, **9**, 204, 215; *J. Amer. Chem. Soc.*, 1940, **62**, 497, 1247; E. S. Barr and G. J. Craven, *J. Chem. Physics*, 1939, **7**, 8.

⁸⁸ *Ibid.*, 1940, **8**, 577; *Trans. Faraday Soc.*, 1940, **36**, 333, 1114.

⁸⁹ *J. Chem. Physics*, 1940, **8**, 349.

⁹⁰ *Ibid.*, 1939, **7**, 857.

⁹¹ *Z. physikal. Chem.*, 1939, **B**, **44**, 299; 1940, **B**, **46**, 229; **B**, **49**, 309; see also O. Wulf and E. J. Jones, *J. Chem. Physics*, 1940, **8**, 745, 753; and L. Zumwalt and R. M. Badger, *J. Amer. Chem. Soc.*, 1940, **62**, 305.

⁹² H. T. Hayes and L. Hunter, *J.*, 1941, 3.

INORGANIC CHEMISTRY.

1. INTRODUCTION AND GENERAL.

THE general arrangement of this Report is the same as in past years. Two topics have been selected for special treatment. The first deals with recent developments in the chemistry of the carbonyls and nitrosyls. Though this subject was discussed in the Annual Reports for 1934 much new research has been published since, many of the developments being based on application of high-pressure technique to the production of carbonyls. The second topic, isotope exchange in inorganic chemistry, is one which is of growing importance in several fields. Radioactive isotopes of all the elements exist, many of them being of suitable half-period for exchange work, while useful methods of separating non-radioactive isotopes have also been worked out. The potential value of this method of studying problems in inorganic chemistry is, therefore, very great.

The first section of the Report deals with a comparatively small number of recent investigations in scattered fields. No detailed discussion is given of papers on complex salts, but attention may be directed to the Bakerian Lecture on Stereochemical Types and Valency Groups¹ and to the Liversidge Lecture on Complex Formation.² These two lectures present a systematic basis for the formulation of a wide range of compounds and are a contribution which is of major importance in the development of the theory of valency. A further publication of wide interest is the Report of the Committee for the Reform of Inorganic Chemical Nomenclature.³ The recommendations made cover specifically many points which at present are confusing, though in the majority of cases they call for no departure from common practice.

A compound of xenon with phenol having the composition Xe_2PhOH has been prepared by B. A. Nikitin.⁴ This has a dissociation pressure of 760 mm. at 4° , its stability being approximately 0.3 of that of the compound $\text{H}_2\text{S}_2\text{PhOH}$. This work follows earlier investigations by the same author in which indications of compound formation by radon were obtained.⁵

Brief reference was made in the Annual Reports for 1940 to an entirely new group of boron hydride derivatives, the metallo-borohydrides. Details of the preparation and properties of three substances of this type were published at the end of 1940.⁶ The table on p. 66 shows their formulæ, melting points, and boiling points, together with data for diborane.

¹ N. V. Sidgwick and H. M. Powell, *Proc. Roy. Soc.*, 1940, **A**, 176, 153.

² N. V. Sidgwick, *J.*, 1941, 433.

³ W. P. Jorissen, H. Bassett, A. Damiens, F. Fichter, and H. Remy, *J.*, 1940, 1404; *J. Amer. Chem. Soc.*, 1941, **63**, 889.

⁴ *Compt. rend. Acad. Sci. U.R.S.S.*, 1940, **29**, 571.

⁵ *Ibid.*, 1939, **24**, 565.

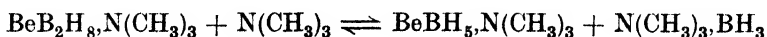
⁶ H. I. Schlesinger, R. T. Sanderson, and A. B. Burg, *J. Amer. Chem. Soc.*, 1940, **62**, 3421; A. B. Burg and H. I. Schlesinger, *ibid.*, p. 3425; H. I. Schlesinger and H. C. Brown, *ibid.*, p. 3429.

Formula.	B ₂ H ₆ .	AlB ₃ H ₁₂ .	BeB ₂ H ₈ .	LiBH ₄ .
M. p.	— 165·5°	— 64·5°	123°	275°
B. p.	— 92·5°	44·5°	91·3°	decomp. 275°
V. p. at 0°, mm.	very high	119	0·5	< 10 ⁻⁵

The first of these compounds, aluminium borohydride, was prepared by heating diborane with trimethylaluminium at 60° for several hours. In the preparation of the beryllium compound an unstable intermediate product of the approximate formula $\text{CH}_3\cdot\text{Be}\cdot\text{BH}_4$ was first produced by the interaction of dimethylberyllium and diborane. Subsequent reaction of this with further diborane gave beryllium borohydride, BeB_2H_8 , together with a non-volatile by-product of the empirical formula BeBH_5 . The lithium borohydride was prepared directly by the reaction of ethyl-lithium and diborane. The only other major products in these reactions were the boron alkyls. The technique employed throughout was similar to that used in earlier investigations of the boron hydrides by Schlesinger and his co-workers and was based largely on methods developed by A. Stock.

There are interesting differences in the physical properties of the three borohydrides. For instance, the relatively high melting point and low volatility of the lithium compound, together with its insolubility in benzene, suggest at once that the bonding is polar in character. The volatility of aluminium borohydride and its ready solubility in benzene show that it is probably non-polar and may be classed with diborane itself. The beryllium compound is intermediate in type, but the indications are that it is more akin to lithium borohydride.

This difference in properties is borne out by the chemical behaviour, for lithium borohydride, unlike diborane, is stable in dry air at ordinary temperatures whereas the aluminium compound is spontaneously inflammable, as is diborane. The beryllium compound also reacts very readily with air. The reactions of these various molecules with trimethylamine again exhibit a striking gradation. Diborane and trimethylamine react at temperatures down to -100° , yielding $\text{BH}_3\cdot\text{N}(\text{CH}_3)_3$. Aluminium borohydride reacts at -80° to 25° , and although the changes are complex and have not been fully elucidated, the crystalline compound $\text{AlB}_3\text{H}_{12}\cdot\text{N}(\text{CH}_3)_3$ has been isolated from the products of reaction of equimolecular quantities at -80° . When heated to 100° this breaks up and borine trimethylamine, $\text{BH}_3\cdot\text{N}(\text{CH}_3)_3$, has been identified as one of the products. At -80° compounds containing a higher molecular proportion of trimethylamine are formed. Beryllium borohydride forms the addition compound $\text{BeB}_2\text{H}_8\cdot\text{N}(\text{CH}_3)_3$ with trimethylamine and this reacts further with the amine according to the equation

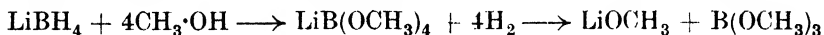


Lithium borohydride, on the other hand, does not react with trimethylamine, a fact which emphasises the difference between this compound and the aluminium and beryllium borohydrides.

The ionic character of lithium borohydride is further supported by the rapid reaction of a benzene solution of aluminium borohydride with ethyl-

lithium to produce lithium borohydride as a white precipitate. This appears to be an ionic double decomposition. The suggestion is made that all three of the borohydrides contain the $[\text{BH}_4]^-$ ion, but that it undergoes a certain amount of distortion. This is a minimum in the lithium compound, and is greatest under the influence of the smaller and more highly charged aluminium ion, with the result that the aluminium compound approximates to the covalent type. The configuration of $\text{AlB}_3\text{H}_{12}$ has been determined by electron diffraction,⁷ and it is found that the aluminium atom and the three BH_4 groups are coplanar with angles of 120° between the Al-B bonds. The compounds $\text{Al}(\text{BH}_4)_3$, $\text{Be}(\text{BH}_4)_2$, and LiBH_4 have each a two-electron deficit per BH_4 group and the B-H distances are greater than those expected for electron-pair bonds. They are equal, in fact, to the distances in diborane, tetraborane, and pentaborane, and there is little doubt that the constitution of the borohydrides can be considered in terms of the theory of resonance in the same manner as that of other boron hydrides.

A number of reactions of the borohydrides have been studied by Schlesinger, Burg, and their co-workers. All are readily hydrolysed. They also react with hydrogen chloride at -80° , producing hydrogen, diborane, and the metal chloride. The aluminium compound was shown to undergo a complex reaction with ammonia, and it also reacted with dimethyl ether to form the compound $\text{AlB}_3\text{H}_{12}\text{O}(\text{CH}_3)_2$, which decomposed at 50° . Lithium borohydride reacted with methyl alcohol according to the equation



A derivative of the type $\text{Li}(\text{BR}_4)$ was obtained by the interaction of ethyl-lithium with trimethylboron, either in presence or in absence of a solvent. A white crystalline product with the formula $\text{LiB}(\text{CH}_3)_3\text{C}_2\text{H}_5$ resulted. It is evident that there are many aspects of these investigations in which important progress may be expected as the experiments are extended.

The association of the alkyls of aluminium, gallium, and indium in the vapour phase has been studied by vapour-density determinations.⁸ Trimethylaluminium proved to be anomalous in that the vapour consists of the dimer at 70° . It dissociates with increase of temperature up to 150° , at which point decomposition sets in. Triethylaluminium is 12% associated to the dimer at 150° . Trimethylgallium and trimethylindium were found to yield monomeric vapours, and the trimethyl and triethyl derivatives of boron are also known to be monomeric.⁹ The monomeric character of trimethylindium is also shown by electron-diffraction measurements.¹⁰

The oxychlorides of silicon have been reinvestigated by W. C. Schumb and D. F. Holloway.¹¹ These compounds, which hitherto were ill defined,

⁷ J. Y. Beach and S. H. Bauer, *J. Amer. Chem. Soc.*, 1940, **62**, 3440.

⁸ A. W. Laubengayer and W. F. Gilliam, *ibid.*, 1941, **63**, 477.

⁹ A. Stock and F. Zeidler, *Ber.*, 1921, **54**, 531.

¹⁰ L. Pauling and A. W. Laubengayer, *J. Amer. Chem. Soc.*, 1941, **63**, 480.

¹¹ *Ibid.*, p. 2753.

were prepared by the action of a mixture of chlorine and oxygen on crystalline silicon at a dull red heat. The reaction product on fractionation yielded compounds of the formulæ $(\text{SiOCl}_2)_4$, Si_2OCl_6 , $\text{Si}_3\text{O}_2\text{Cl}_8$, $\text{Si}_4\text{O}_3\text{Cl}_{10}$, $\text{Si}_5\text{O}_4\text{Cl}_{12}$, $\text{Si}_6\text{O}_5\text{Cl}_{14}$ and $\text{Si}_7\text{O}_6\text{Cl}_{16}$. The first was a crystalline solid, the others being liquids of low volatility, all of which were of the type $\text{Si}_n\text{O}_{n-1}\text{Cl}_{2n+2}$, and were analogous to the oxybromides of silicon.¹²

Reaction of these oxychlorides with absolute alcohol has so far yielded the following esters: $\text{Si}_2\text{O}(\text{OC}_2\text{H}_5)_6$, $\text{Si}_3\text{O}_2(\text{OC}_2\text{H}_5)_8$, $\text{Si}_4\text{O}_3(\text{OC}_2\text{H}_5)_{10}$ and $\text{Si}_5\text{O}_4(\text{OC}_2\text{H}_5)_{12}$. These are non-inflammable high-boiling liquids which resist hydrolysis by water at 100° . In an extension of these investigations hexacyclohexyloxydisiloxane, $(\text{C}_6\text{H}_{11}\text{O})_3\text{Si}-\text{O}-\text{Si}(\text{C}_6\text{H}_{11}\text{O})_3$, has been prepared from cyclohexanol and the oxychloride Si_2OCl_6 .¹³

Attempts to prepare silicon compounds of the type $\text{SiR}_3\cdot\text{SiR}_3$ and $\text{SiR}_3\cdot\text{O}\cdot\text{SiR}_3$ from the corresponding silicon halides by the Wurtz synthesis normally lead to fission of the Si-Si or Si-O-Si bonds. It has been found, however, that by first preparing the sodium compound from an aryl halide and then allowing it to react with the silicon halide, compounds of the required type may be obtained.¹⁴ For example, phenylsodium, prepared from chlorobenzene and sodium, reacts with Si_2OBr_6 to yield $(\text{C}_6\text{H}_5)_6\text{Si}_2\text{O}$, and Si_2Cl_6 gives hexaphenyldisilane.

Polymers derived from methylsilicon oxides have assumed considerable importance during the past year owing to the possibility of their technical application. The simplest starting materials for preparing such polymers are the methylsilicon chlorides, which have been described by W. F. Gilliam, H. A. Liebhafsky, and A. F. Winslow.¹⁵ Dimethylsilicon dichloride and methylsilicon trichloride are formed by the interaction of methylmagnesium chloride and silicon tetrachloride in the appropriate proportions. The products were fractionally distilled and the boiling points of the two halides in an approximately pure state were found to be $69.0\text{--}70.2^\circ$ and $66.2\text{--}67.0^\circ$, respectively. These values are anomalous in that they lie outside the range fixed by the boiling points of tetramethylsilicon and silicon tetrachloride.

Polymeric methylsilicon oxides may be produced by hydrolysis of either the separated or the mixed alkylsilicon halides.¹⁶ In either case the halogen compound, dissolved in ether, was poured on ice. The resulting methylsilicols dissolved in the ether and remained on evaporation of the solvent as a syrup which could be hardened. With an average of $1.0\text{--}1.3$ methyl groups per silicon atom, the condensation proceeded at room temperature through a sticky, syrupy stage to a hard, transparent resin, which became brittle when warmed. With a ratio of $1.3\text{--}1.5$, the product at room temperature was an oily liquid, the viscosity of which increased with rising temperature until at $150\text{--}200^\circ$ gelation occurred in a few hours. The gel

¹² W. C. Schumb and C. H. Klein, *J. Amer. Chem. Soc.*, 1937, **59**, 261.

¹³ W. C. Schumb and D. F. Holloway, *ibid.*, 1941, **63**, 2853.

¹⁴ W. C. Schumb and C. M. Saffer, jun., *ibid.*, p. 93.

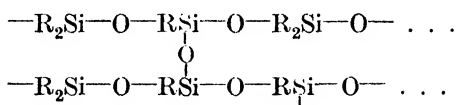
¹⁵ *Ibid.*, p. 801.

¹⁶ E. G. Rochow and W. F. Gilliam, *ibid.*, p. 798.

then set gradually to a transparent, horny resin. With $\text{CH}_3:\text{Si}$ ratios of 1.5—1.9 a gel formed in a few hours at 200° , and this product became brittle only when heated for several weeks at 200° . With a $\text{CH}_3:\text{Si}$ ratio of 1.3—1.5 the initial condensation products were soluble in hydrocarbons or alcohols, although the fully hardened resin was insoluble and infusible. The hardened resin had a high thermal stability; *e.g.*, when a sample was heated in air for a year at 200° no perceptible change occurred. At 300° in air surface oxidation took place. Samples heated for 16 hours in a vacuum at 550° or for 1 hour in hydrogen at 450° suffered only a discolouration.

A further investigation on this important group of compounds has been published by J. F. Hyde and R. C. DeLong.¹⁷ These authors studied the hydrolysis of phenylethyl-, phenylmethyl-, diphenyl-, diethyl-, and dimethyl-dichlorosilanes. The products were liquid except those from the diphenyl compound, the diol from which was a crystalline solid. This when treated in hot alcoholic solution with dilute ammonia or dilute sodium hydroxide was converted into a cyclic trimer, which was characterised. When the liquid hydrolysis products of the compounds containing phenyl groups were treated at high temperatures with aqueous hydrochloric acid there was a gradual increase in viscosity, accompanied by evolution of benzene. The ultimate product was an insoluble resin. The dialkyl derivatives were found, in general, to be more gel-like than those containing a phenyl group, but they had less physical strength after curing than the latter. All films formed from solutions of the various resins lost their tackiness and solubility with appropriate baking. The final products resembled films formed by drying oils, though they were superior in thermal stability.

There is at present an insufficient basis for discussion of the constitution of these polymers, but E. G. Rochow and W. F. Gilliam¹⁸ suggest that the cross-linked siloxane structure shown below probably represents an essential part.



Two new iodo-derivatives of monosilane, *viz.*, SiH_3I and SiH_2I_2 , have been prepared by the interaction of dry hydrogen iodide and monosilane in the presence of aluminium tri-iodide, which acts as a catalyst.¹⁸ The boiling points are 45.4° and 149.5° , respectively. Neither of the compounds is spontaneously inflammable in air, although both burn readily. In moist air, simultaneous oxidation and hydrolysis take place. Silyl iodide, SiH_3I , reacts with mercury in sunlight, yielding mercurous iodide, silane, and disilane. The liquid iodide and mercury in absence of sunlight form an unstable, white, crystalline solid which decomposes into mercurous iodide and silane. This may be mercurysilyl iodide, $\text{SiH}_3\cdot\text{HgI}$. There is a similar reaction with zinc. With magnesium in diisomyl ether there is strong

¹⁷ *J. Amer. Chem. Soc.*, 1941, **63**, 1194.

¹⁸ H. J. Emeléus, A. G. Maddock, and C. Reid, *J.*, 1941, 353.

evidence that a Grignard compound is produced, and treatment of this with water gives monosilane. Liquid silyl iodide reacts explosively with silver cyanide, forming silver iodide and a brown polymeric solid. By passing the vapour of silyl iodide over silver cyanide at room temperature the compound SiH_3CN , m. p. 34° , is produced. Silyl iodide reacts with sodium, forming disilane.

The reducing action of sodium, potassium, or calcium on liquid ammonia solutions of nickel salts has been shown to yield free nickel.¹⁹ The metal is pyrophoric and catalyses further reaction between alkali or alkaline-earth metal and ammonia. Small amounts of nickel amide may also be formed.

Nitroxyl perchlorate, NClO_6 , has been prepared by the controlled interaction of chlorine dioxide and an air stream containing ozone and nitrogen oxides.²⁰ It is a white crystalline solid with a vapour pressure less than 0.05 mm. at room temperature. It decomposes at 120° and reacts violently with most organic liquids. Reaction with water yields a mixture of nitric and perchloric acids, and the compound is regarded as a mixed anhydride of these two acids.

The direct oxidation of phosphorus tribromide to the oxybromide by means of oxygen is not readily controlled and is liable to occur explosively, in which case phosphoric oxide and free bromine are among the products. It has been shown, however, that under the catalytic influence of nitrogen dioxide and with carefully controlled reaction conditions a smooth reaction may be obtained.²¹ The direct preparation of phosphorus-halogen compounds from phosphoric oxide and metal halides has also been reported.²² When mixtures of phosphoric oxide and calcium fluoride are heated to 550° , phosphorus oxyfluoride is the chief volatile product. In iron vessels a certain amount of reduction to the trifluoride also takes place. When mixtures of calcium fluoride and sodium chloride were used, the products were PF_3 , POF_3 , POF_2Cl , POFCl_2 , and POCl_3 . In these reactions the hitherto unknown difluorophosphoric acid, HPO_2F_2 , which was probably formed by partial hydrolysis of phosphorus oxyfluoride, was also isolated.

In a group of publications dealing with polyiodides of the alkali metals, T. R. Briggs and his co-workers report extensive phase-rule studies.²³ In the system sodium iodide-iodine-water they obtained the three polyiodides Na_4I_{14} , 13–15 H_2O , Na_5I_{11} , 17–19 H_2O , and Na_6I_8 , 10–11 H_2O . There was no indication of a solid tri-iodide. Similar studies with rubidium iodide showed the existence of anhydrous RbI_3 , and in the system caesium iodide-iodine-water the existence of the two binary compounds, CsI_3 and CsI_4 , was established. Two compounds of the formulæ $\text{KI}_3\cdot\text{C}_6\text{H}_6$ and $\text{KI}_5\cdot 2\text{C}_6\text{H}_6$

¹⁹ W. M. Burgess and J. W. Eastes, *J. Amer. Chem. Soc.*, 1941, **63**, 2674.

²⁰ W. E. Gordon and J. W. T. Spinks, *Canadian J. Res.*, 1940, **18**, B, 358.

²¹ C. R. Johnson and L. G. Nunn, jun., *J. Amer. Chem. Soc.*, 1941, **63**, 141.

²² G. Tarbutton, E. P. Egan, jun., and S. G. Frary, *ibid.*, p. 1782.

²³ T. R. Briggs, W. F. Geigle, and J. L. Eaton, *J. Physical Chem.*, 1941, **45**, 595; T. R. Briggs, C. C. Conrad, C. C. Gregg, and W. H. Reed, *ibid.*, p. 614; T. R. Briggs and S. S. Hubbard, *ibid.*, p. 806.

have been prepared by the addition of potassium iodide to a saturated solution of iodine in benzene.²⁴

In a study of the action of chlorine on hydroxides of lithium and potassium in presence of iodine, R. K. Bahl and S. Singh²⁵ have shown that the product from a boiling solution of iodine in lithium hydroxide is $\text{Li}_8\text{I}_2\text{O}_{11} \cdot 2\text{H}_2\text{O}$, whereas potassium hydroxide under similar conditions gives KIO_4 . When chlorine is passed into hot solutions of barium or strontium hydroxide, or a hot suspension of calcium hydroxide, containing dissolved iodine, the iodates $\text{Ba}(\text{IO}_3)_2 \cdot \text{H}_2\text{O}$, $\text{Sr}(\text{IO}_3)_2 \cdot \text{H}_2\text{O}$ and $\text{Ca}(\text{IO}_3)_2 \cdot \text{H}_2\text{O}$ are precipitated, no periodate being formed.

H. J. E.

2. METALLIC CARBONYLS AND NITROSYLS.

Since the chemistry of the carbonyls and nitrosyls was last discussed in these Reports¹ a number of notable developments in this field have been reported. Some of these have already been reviewed,^{2,3} but a general survey including details of the most recent advances is opportune.

The known metallic carbonyls, carbonyl hydrides, and carbonyl halides are listed in the table on p. 72. Of these compounds the most accessible are nickel tetracarbonyl and iron pentacarbonyl, both liquids under normal temperature and pressure conditions, which are obtained on the commercial scale by the direct action of carbon monoxide on the finely-divided metals.^{2,3} Nickel tetracarbonyl is unique in that it is prepared in excellent yield by this direct method without the use of high pressures; "dry" methods for the preparation of the other carbonyls, including iron pentacarbonyl (from which the other iron carbonyls⁴ and the tetracarbonyl hydride are prepared), require the use of high-pressure technique, and it is to the systematic application of this technique that many of the recent advances are due.

The high-pressure apparatus and methods used by W. Hieber and his collaborators in their more recent studies on the carbonyls have been described.⁵ The rotating autoclave and auxiliary apparatus are designed to withstand pressures up to 350 atm. The chief constructional difficulty lies in the choice of material for those parts of the apparatus which come into contact with carbon monoxide under pressure; alloys containing iron, nickel, etc., cannot be used since these metals combine readily with carbon monoxide to form their carbonyls. Copper-silver alloys have been found to be most suitable for the autoclave lining; pure copper can be used at temperatures up to 200°, but above this temperature

²⁴ J. A. Fialkov and A. B. Polischtschuk, *Ber. Inst. Chem. Akad. Wiss. Ukrain.*, 1940, **7**, 95.

²⁵ *J. Indian Chem. Soc.*, 1940, **17**, 167, 397.

¹ W. Wardlaw, *Ann. Reports*, 1934, **31**, 99.

² W. Hieber, *Z. Elektrochem.*, 1937, **43**, 390.

³ A. A. Blanchard, *Chem. Reviews*, 1937, **21**, 3.

⁴ E. Speyer and H. Wolf, *Ber.*, 1927, **60**, 1424 [$\text{Fe}_2(\text{CO})_9$]; W. Hieber, *Z. anorg. Chem.*, 1932, **204**, 165 [$(\text{Fe}(\text{CO})_5)_2$].

⁵ W. Hieber, H. Schulten, and R. Marin, *ibid.*, 1939, **240**, 261.

the various components become welded together and the apparatus cannot be dismantled. The high-pressure technique used in the preparation of the ruthenium carbonyls has also been described.⁶

Metallic Carbonyls, Carbonyl Hydrides, and Carbonyl Halides.

	Element.	At. no.	Carbonyls.	Carbonyl hydrides.	Carbonyl halides.
Group VI	$\begin{Bmatrix} \text{Cr} \\ \text{Mo} \end{Bmatrix}$	$\begin{matrix} 24 \\ 42 \end{matrix}$	$\begin{matrix} \text{Cr}(\text{CO})_6 \\ \text{Mo}(\text{CO})_6 \end{matrix}$		
	$\begin{Bmatrix} \text{W} \\ \text{Re} \end{Bmatrix}$	$\begin{matrix} 74 \\ 75 \end{matrix}$	$\begin{matrix} \text{W}(\text{CO})_6 \\ [\text{Re}(\text{CO})_5]_2^a \end{matrix}$		
Group VII	Fe	26	$\begin{matrix} \text{Fe}(\text{CO})_5 \\ \text{Fe}_2(\text{CO})_9 \\ [\text{Fe}(\text{CO})_4]_3 \end{matrix}$	$\text{H}_2\text{Fe}(\text{CO})_4$	$\begin{matrix} \text{Re}(\text{CO})_5\text{X} \\ \text{Fe}(\text{CO})_5\text{X}_2 \\ \text{Fe}(\text{CO})_4\text{X}_2 \\ \text{Fe}(\text{CO})_2\text{X}_2 \\ \text{Fe}(\text{CO})_2\text{X} \\ [\text{Fe}(\text{CO})_3\text{X}_2]_3^b \\ \text{Co}(\text{CO})\text{X}_2 \end{matrix}$
	Co	27	$\begin{matrix} [\text{Co}(\text{CO})_4]_2 \\ [\text{Co}(\text{CO})_3]_4 \end{matrix}$	$\text{HCo}(\text{CO})_4$	
	Ni	28	$\text{Ni}(\text{CO})_4$		
Group VIII	Ru	44	$\begin{matrix} \text{Ru}(\text{CO})_5 \\ \text{Ru}_2(\text{CO})_9 \\ [\text{Ru}(\text{CO})_4]_n \end{matrix}$	$\text{H}_2\text{Ru}(\text{CO})_4?$	$\begin{matrix} \text{Ru}(\text{CO})_5\text{X}_2^c \\ \text{Ru}(\text{CO})\text{X}^d \end{matrix}$
	Rh	45			$\text{Rh}(\text{CO})_3\text{X}_2, \text{RhO}^*$
	Pd	46			$\text{Pd}(\text{CO})\text{X}_2^f$
	Os	76	$\text{Os}(\text{CO})_6^g$		$\text{Os}(\text{CO})_3\text{X}_2^h$
	Ir	77	$\begin{matrix} [\text{Ir}(\text{CO})_4]_n \\ [\text{Ir}(\text{CO})_3]_n \end{matrix}$	$\text{HIr}(\text{CO})_4?$	$\begin{matrix} \text{Ir}(\text{CO})_3\text{X} \\ \text{Ir}(\text{CO})_2\text{X}_2 \\ \text{Pt}(\text{CO})_3\text{X}_2^i \\ \text{Pt}_2(\text{CO})_3\text{X}_2^j \\ \text{Pt}(\text{CO})\text{X}_2 \\ \text{Cu}(\text{CO})\text{X} \\ \text{Au}(\text{CO})\text{X}^j \end{matrix}$
	Pt	78			
Group I	$\begin{Bmatrix} \text{Cu} \\ \text{Au} \end{Bmatrix}$	$\begin{matrix} 29 \\ 79 \end{matrix}$			

Notes :

(a) In the table X represents chlorine, bromine, or iodine; metallic carbonyl fluorides have not yet been reported.

(b) Compounds to which references are not appended are referred to in the text of this Report.

^a Details not yet available; cf. W. Hieber, *Z. anorg. Chem.*, 1941, **248**.

^b *Idem, ibid.*, 1931, **201**, 329.

^c W. Manchot and J. König, *Ber.*, 1924, **57**, 2130.

^d W. Manchot and E. Enk, *ibid.*, 1930, **63**, 1635.

^e W. Manchot and J. König, *ibid.*, 1925, **58**, 2173.

^f *Idem, ibid.*, 1926, **59**, 883.

^g Reported by W. Hieber; work not yet published.

^h W. Manchot and J. König, *Ber.*, 1925, **58**, 229.

ⁱ P. Schützenberger, *Bull. Soc. chim.*, 1868, [ii], **10**, 188; *Ann. Chim. Phys.*, 1868, [iv], **15**, 100; 1870, [iv], **21**, 350.

^j W. Manchot and H. Gall, *Ber.*, 1925, **58**, 2175.

The direct preparation of cobalt tetracarbonyl from cobalt and carbon monoxide is inconvenient, since carefully reduced cobalt must be employed. The methods of Schubert and of Coleman and Blanchard⁷ use readily accessible materials, but give relatively small yields. These disadvantages

⁶ W. Manchot and W. J. Manchot, *Z. Anorg. Chem.*, 1936, **226**, 385; cf. also W. Hieber and H. Fischer, D.R.-P. 695,589 (1940), for ruthenium carbonyls.

⁷ Cf. p. 76, refs. (18) and (19).

are overcome in Hieber's method,⁵ in which cobalt sulphide is heated at 200° with carbon monoxide under 200 atm. pressure; the reaction proceeds quantitatively according to the equation $2\text{CoS} + 8\text{CO} + 4\text{Cu} \longrightarrow [\text{Co}(\text{CO})_4]_2 + 2\text{Cu}_2\text{S}$. The copper required in this reaction is obtained from the autoclave lining, or from copper powder added to the cobalt sulphide. The carbonyl is extracted from the solid products with an organic solvent. If water is present in the reacting materials, considerable yields of the volatile cobalt tetracarbonyl hydride, $\text{HCo}(\text{CO})_4$, are obtained; this hydride can also be prepared by high-pressure synthesis from (a) cobalt sulphide, carbon monoxide, and hydrogen; (b) cobalt tetracarbonyl and hydrogen; (c) cobalt, carbon monoxide, and hydrogen; or (d) cobalt hydride (CoH_2) and carbon monoxide.

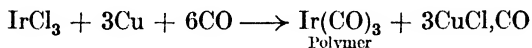
The action of carbon monoxide at high pressures on cobaltous halides in presence of certain other metals also affords cobalt tetracarbonyl, or, in presence of water or hydrogen, the tetracarbonyl hydride.⁵ The conditions and mechanism of formation of the tetracarbonyl by this process have been studied in some detail.⁸ Cobaltous iodide is completely converted into the carbonyl by heating at 150° for 15 hours with carbon monoxide under 200 atm. pressure; the bromide and chloride give small yields of the carbonyl at 200—300°, but the fluoride does not react. The halogen is eventually eliminated from the reaction by combination with copper in the autoclave wall: $2\text{CoI}_2 + 4\text{Cu} + 8\text{CO} \longrightarrow [\text{Co}(\text{CO})_4]_2 + 4\text{CuI}$. This mode of reaction persists even if direct contact between the cobaltous halide and the autoclave is prevented by a glass sleeve, showing that some volatile intermediate is involved. In the case of cobaltous iodide this intermediate is probably $\text{Co}(\text{CO})\text{I}_2$, which can be obtained as brownish-black crystals by the action of carbon monoxide at 100—400 atm. on the anhydrous iodide, at room temperature; $\text{Co}(\text{CO})\text{I}_2$ has a high dissociation pressure of carbon monoxide and decomposes in a few seconds at normal temperatures and pressures. The yields of cobalt tetracarbonyl obtained from cobaltous bromide or chloride and carbon monoxide are considerably increased by mixing a metal powder with the halide in order to facilitate elimination of the halogen. The effectiveness of the metals tried decreases in the order copper, silver, platinum, gold; the heats of formation of the appropriate halides also decrease in this order, showing that a controlling factor in the formation of the carbonyl is the reaction between the solid cobaltous halide and the admixed metal, e.g., $\text{CoBr}_2 + 2\text{Ag} \longrightarrow \text{Co} + 2\text{AgBr}$. If argon is substituted for carbon monoxide, reactions of this type give equilibrium mixtures containing relatively little cobalt; this indicates that carbon monoxide plays an essential part in the reaction between the metal and the halide, and does not merely combine with free cobalt formed in an independent reaction. The use of a more electropositive metal, such as zinc or cadmium, leads to the formation of a crystalline, appreciably volatile "mixed carbonyl" of the metal and cobalt, probably to be regarded as a derivative of cobalt carbonyl hydride, e.g., $\text{Zn}[\text{Co}(\text{CO})_4]_2$. It is stated⁸

* W. Hieber and H. Schulten, *Z. anorg. Chem.*, 1939, **243**, 145.

that reactions corresponding with those described above also occur with nickel and iron halides.

Cobalt tricarbonyl, $[\text{Co}(\text{CO})_3]_4$, is readily obtained by heating the tetracarbonyl at about 52° .⁹

Although a dicarbonyl chloride of iridium, $\text{Ir}(\text{CO})_2\text{Cl}_2$, has been known for some time,¹⁰ simple carbonyls of iridium have not been described until recently. The tricarbonyl, $[\text{Ir}(\text{CO})_3]_n$, has been prepared by the action of carbon monoxide at 200 atm. pressure on a trihalide of iridium.¹¹ The halogen is again eliminated by combination with copper from the autoclave lining :



The chloride, bromide, and iodide react in this way at 140° , 110 – 120° , and 90 – 100° , respectively; conversion of the trichloride into the carbonyl is complete after 24–48 hours at 140° . The product can be sublimed in carbon monoxide at 200 – 210° . In this reaction, actual addition of a halogen-absorbing metal, such as copper or silver, is avoided, since immediate reduction of the iridium halide to metallic iridium would occur on heating to the requisite temperature, and the iridium would not react with carbon monoxide under the conditions given. If complex iridium halides, such as K_2IrBr_6 , are used instead of the trihalides, addition of copper or silver is, however, necessary if the halogen is to be displaced completely; K_2IrBr_6 and carbon monoxide, without added metal, give a new carbonyl halide, $\text{Ir}(\text{CO})_3\text{Br}$. Although the tricarbonyl is the main product of the reaction of iridium trihalides and carbon monoxide, the complex halides (with copper or silver) give mixtures of the yellow tricarbonyl and a greenish-yellow crystalline tetracarbonyl, $[\text{Ir}(\text{CO})_4]_n$; the mixtures can be separated by extraction with carbon tetrachloride or ethyl ether, in which the tetracarbonyl is slightly soluble, or by fractional sublimation, the tetracarbonyl subliming at about 160° in carbon monoxide at normal pressure. Iridium tetracarbonyl is very readily converted into the tricarbonyl, which is sufficiently stable to resist attack by concentrated acids, dilute alkalis, or free halogens at room temperature. The molecular weights of the iridium carbonyls could not be determined owing to their low solubility; the properties of the tetracarbonyl are consistent with the dimeric formula, $[\text{Ir}(\text{CO})_4]_2$ (indicated by analogy with the cobalt compounds), whereas the tricarbonyl is clearly more complex ($[\text{Ir}(\text{CO})_3]_4$?) since it is less volatile and less soluble.

The formation of cobalt tetracarbonyl hydride from cobalt compounds, carbon monoxide, and substances containing hydrogen has been noted above. Apparently an iridium carbonyl hydride, probably $\text{HIr}(\text{CO})_4$, is formed under similar conditions, for the action of carbon monoxide on iridium trihalides in presence of water or hydrogen affords a volatile and very unstable substance containing iridium; this gives a colourless solid

⁹ W. Hieber, F. Mühlbauer, and E. A. Ehmann, *Ber.*, 1932, **65**, 1090.

¹⁰ W. Manchot and H. Gall, *ibid.*, 1925, **58**, 232.

compound with mercuric chloride solution.¹¹ It appears, therefore, that a close analogy exists between the carbonyl derivatives of cobalt and iridium.

The hexacarbonyls of chromium, molybdenum, and tungsten were first prepared in quantities sufficient for analysis by the action of carbon monoxide and a Grignard reagent on the anhydrous halides of the metals.¹² The yields obtained by this method are small. Molybdenum and tungsten hexacarbonyls are better prepared by treating the reduced metal with carbon monoxide (at 200 atm. and about 225°) in presence of another metal (e.g., copper or iron);¹³ these carbonyls have also been obtained by treating the chlorides or bromides of the metals, or corresponding complex salts (e.g., K_3MoCl_6 , $K_3W_2Cl_9$), with carbon monoxide under pressure, in presence of a metal to remove the halogen.¹⁴ Chromium hexacarbonyl apparently cannot be prepared by either of these methods, and only the original method of Job¹² is available in this case. The hexacarbonyls of the Group VI metals, which are colourless crystalline solids, are considerably more stable than the simpler carbonyls of the Group VIII elements, probably because the attainment of the effective atomic number of a rare gas by the central metal atom coincides with the formation of the inherently stable six-coordinate complex.

Brief reference has already been made to the tetracarbonyl hydrides of iron, cobalt, and iridium; it appears likely that a similar compound of ruthenium [presumably $H_2Ru(CO)_4$], maintaining the analogy between ruthenium and iron] also exists, since ruthenium pentacarbonyl reacts with alkalis to give fairly stable solutions with strong reducing properties,⁶ just as iron pentacarbonyl reacts to give strongly reducing solutions of the iron tetracarbonyl hydride.

Iron and cobalt tetracarbonyl hydrides have been isolated and studied in some detail; they are very volatile liquids, stable only at temperatures well below 0°. The free iron compound was first obtained by Hieber and his collaborators¹⁵ by the action of an aqueous solution of a base (preferably barium hydroxide) on iron pentacarbonyl, followed by acidification of the solution. A similar reaction with cobalt tetracarbonyl affords free cobalt tetracarbonyl hydride.^{16, 17}

Several reactions have now been studied in which cobalt tetracarbonyl hydride derivatives are obtained by the action of carbon monoxide on solutions (or suspensions) of cobalt salts. These reactions take place at

¹¹ W. Hieber and H. Lagally, *Z. anorg. Chem.*, 1940, **245**, 321.

¹² A. Job and A. Cassal, *Compt. rend.*, 1926, **183**, 58, 392; *Bull. Soc. chim.*, 1927, [iv], **41**, 1041; A. Job and J. Rouvillois, *Compt. rend.*, 1928, **187**, 564; W. Hieber and E. Romberg, *Z. anorg. Chem.*, 1935, **221**, 321.

¹³ I. G. Farbenindustrie A.-G., F.P. 708,379, 708,260 (1930); B.P. 367,481 (1930); D.R.-P. 547,025 (1931).

¹⁴ W. Hieber *et al.*, details not yet published.

¹⁵ W. Hieber and F. Leutert, *Naturwiss.*, 1931, **19**, 360; *Ber.*, 1931, **64**, 2832; *Z. anorg. Chem.*, 1932, **204**, 145; W. Hieber and H. Vetter, *ibid.*, 1933, **212**, 145.

¹⁶ W. Hieber, *Angew. Chem.*, 1936, **49**, 463.

¹⁷ W. Hieber and H. Schulten, *Z. anorg. Chem.*, 1937, **232**, 17, 29.

normal pressures, and provide means of preparing cobalt tetracarbonyl hydride and the tetracarbonyl (which is readily obtained by decomposition of the hydride on warming) with readily available apparatus and materials. Unfortunately, the reactions are slow and accumulation of moderate quantities of the products is tedious. An alkaline solution of cobalt chloride will not absorb carbon monoxide, but on addition of cysteine to this solution the gas is absorbed, and cobalt tetracarbonyl hydride is liberated on acidification of the resulting liquid.^{18, 19} This reaction probably occurs by the intermediate formation of complexes of cobalt and cysteine containing carbon monoxide; such complexes have not yet been isolated, although iron compounds of a corresponding type are known.¹⁸ A mechanism has been worked out for the above reaction,¹⁸ involving "disproportionation" of a bivalent cobalt complex to a cobalt tetracarbonyl hydride derivative (presumably the alkali salt) and a trivalent cobalt complex; the latter is reduced by carbon monoxide in a subsequent stage of the reaction. Certain other substances, notably tartrates, can replace cysteine in this reaction.¹⁹ Nickel tetracarbonyl is readily prepared by the action of carbon monoxide on an alkaline suspension of nickel cyanide or sulphide,²⁰⁻²² and carbon monoxide is also absorbed by alkaline suspensions of cobalt cyanide or sulphide; cobalt tetracarbonyl or the hydride has not, however, been isolated from the reaction products, although cobalt nitrosyl carbonyl, $\text{Co}(\text{CO})_3\text{NO}$ (see below), has been obtained by passing nitric oxide into the solution.²² An interesting addition compound of cobalt tetracarbonyl, $[\text{Co}(\text{CO})_4]_2\text{EtOH}$, has been prepared by the action of carbon monoxide on an alcoholic solution of cobaltous chloride and potassium ethyl xanthate.²³ In all these processes it appears likely that intermediates containing carbon monoxide are formed, and a further study of the reactions involved may lead to an interesting new branch of carbonyl chemistry. It is noteworthy that linkings between metal and sulphur atoms are, for some reason not yet understood, particularly susceptible to reaction with carbon monoxide.

The tetracarbonyl hydrides of iron and cobalt form an interesting series of crystalline derivatives with complex cations containing ammonia or *o*-phenanthroline (phenan).²⁴ Typical members of the series are $[\text{Ni}(\text{NH}_3)_6][\text{Co}(\text{CO})_4]_2$, $[\text{Mn}(\text{NH}_3)_6][\text{HFe}(\text{CO})_4]_2$, and $[\text{Co}(\text{phenan})_3][\text{Co}(\text{CO})_4]_2$, which are prepared by addition of a solution containing the appropriate complex cation to an ammoniacal solution of the carbonyl hydride. The ammonia compounds are stable in the absence of air, but react readily with ammonia, pyridine, etc., and slowly with methyl alcohol; the *o*-phenanthroline compounds are stable in air and notably less reactive. With

¹⁸ M. P. Schubert, *J. Amer. Chem. Soc.*, 1933, **55**, 4563.

¹⁹ G. W. Coleman and A. A. Blanchard, *ibid.*, 1936, **58**, 2160; cf. also A. A. Blanchard and P. Gilmont, *ibid.*, 1940, **62**, 1192.

²⁰ W. Manchot and H. Gall, *Ber.*, 1929, **62**, 678.

²¹ M. M. Windsor and A. A. Blanchard, *J. Amer. Chem. Soc.*, 1933, **55**, 1877.

²² A. A. Blanchard, J. R. Rafter, and W. B. Adams, *ibid.*, 1924, **56**, 16.

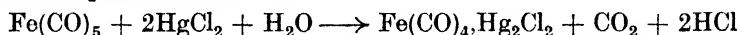
²³ W. Hieber, *Angew. Chem.*, 1936, **49**, 463.

²⁴ W. Hieber and E. Fack, *Z. anorg. Chem.*, 1938, **236**, 83.

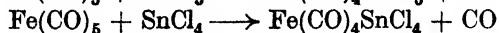
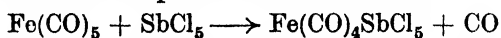
zinc, cadmium, and copper salts the ammoniacal solution of iron tetracarbonyl hydride reacts to give compounds of a different type, *viz.*, $\text{Zn}(\text{NH}_3)_3\cdot\text{Fe}(\text{CO})_4$, $\text{Cd}(\text{NH}_3)_2\cdot\text{Fe}(\text{CO})_4$,²⁵ and $\text{Cu}_2(\text{NH}_3)_3\cdot\text{Fe}(\text{CO})_4$, in which both hydrogen atoms are displaced from the carbonyl hydride. The hexammine and *o*-phenanthroline compounds are regarded by Hieber as true salts of iron tetracarbonyl hydride, since they are shown by electrical conductivity measurements to dissociate in methanol and acetone solutions. The zinc, copper, and cadmium compounds are non-electrolytes, however, and these are considered to be polynuclear complexes which are possibly similar in constitution to substituted carbonyls, such as $\text{Fe}_2(\text{CO})_4(\text{C}_5\text{H}_5\text{N})_3$. Conductivity measurements also show that the free iron and cobalt tetracarbonyl hydrides are dissociated in pyridine solution.

The table given on p. 72 shows the large number of carbonyl halides now known to exist. The properties and reactions of the iron compounds have been studied in considerable detail.²⁶ At low temperatures iron pentacarbonyl adds free halogens to give unstable compounds of the type $\text{Fe}(\text{CO})_5\text{X}_2$; these decompose at temperatures varying from -35° to 0° , more stable tetracarbonyl derivatives, $\text{Fe}(\text{CO})_4\text{X}_2$, being formed. The tetracarbonyl iodide is also formed on treating iron tetracarbonyl hydride with iodine, or by the action of carbon monoxide under high pressure on anhydrous ferrous iodide;²⁷ the kinetics of the latter reaction show certain unusual features. "Mixed" iron tetracarbonyl halides, $\text{Fe}(\text{CO})_4\text{IBr}$ and $\text{Fe}(\text{CO})_4\text{ICl}$, have now been prepared²⁸ by the action of iodine monobromide or monochloride on iron pentacarbonyl; these compounds decompose readily into mixtures of the two simple carbonyl halides. As expected, the "mixed" halides possess, in general, properties intermediate between those of the two corresponding simple carbonyl halides.

The possible reactions of iron pentacarbonyl with halides of metals in their higher states of oxidation have recently been examined.²⁸ The first possible type of reaction, in which part of the carbon monoxide is displaced from the carbonyl and oxidised to carbon dioxide, occurs with mercuric chloride in aqueous solution :²⁹



The compound $\text{Fe}(\text{CO})_4\cdot\text{Hg}_2\text{Cl}_2$ should probably be regarded as a double salt of the mercury derivative of iron tetracarbonyl hydride, $\text{HgFe}(\text{CO})_4\cdot\text{HgCl}_2$; the simple mercury derivative, $\text{HgFe}(\text{CO})_4$, is obtained by using mercuric sulphate instead of the chloride.²⁹ The reactions of iron pentacarbonyl with stannic chloride and antimony pentachloride are of a second type in which carbon monoxide is displaced but not oxidised :



²⁵ Cf. also F. Feigl and P. Krumholz, *Z. anorg. Chem.*, 1933, **215**, 242.

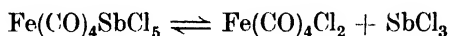
²⁶ W. Hieber *et al.*, *ibid.*, 1930, **190**, 192, 215; 1931, **201**, 329.

²⁷ W. Hieber and H. Lagally, *ibid.*, 1940, **245**, 305.

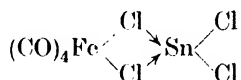
²⁸ W. Hieber and A. Wirsching, *ibid.*, p. 35.

²⁹ H. Hock and H. Stuhlmann, *Ber.*, 1928, **61**, 2097; 1929, **62**, 431, 2690.

The new compounds obtained are shown by their reactions to contain iron in the bivalent condition, with trivalent antimony or bivalent tin. They are more stable than the iron tetracarbonyl halides to which they appear to be related; the antimony compound is dissociated in benzene or nitrobenzene solution :

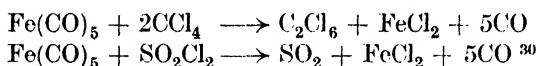


but the tin compound shows a normal molecular weight and is regarded as a binuclear complex :

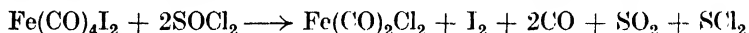


With other halides (*e.g.*, ferric and cupric chlorides) both the above types of reaction appear to occur together, both carbon monoxide and carbon dioxide being evolved; additive compounds analogous to those just described have not, however, been isolated.

Iron pentacarbonyl shows a strong tendency to displace halogens from non-metallic halides, as the following reactions show : ²⁸



In each case an iron carbonyl halide is probably formed as an intermediate product. The corresponding reaction with thionyl chloride is more complex, and affords evidence for the existence of an iron dicarbonyl chloride, $\text{Fe}(\text{CO})_2\text{Cl}_2$; this compound, a reactive, brown, crystalline solid, is isolated by using iron tetracarbonyl iodide instead of iron pentacarbonyl :



The tetracarbonyl bromide reacts in a similar manner. It is noteworthy that a ruthenium dicarbonyl chloride, $\text{Ru}(\text{CO})_2\text{Cl}_2$, analogous to the new iron derivative, has been known for some time.³¹

Although a number of iron carbonyl derivatives containing co-ordinated substituents (amines, etc.) contain from one to four molecules of carbon monoxide per atom of iron,³² the dicarbonyl chloride discussed above is the first known example of a simple iron carbonyl halide with a CO : Fe ratio of less than 4. Further investigation³³ has shown that a similar compound, $\text{Fe}(\text{CO})_2\text{I}_2$, is formed as a product of the thermal decomposition of iron tetracarbonyl iodide in an inert atmosphere; other products, obtained under different conditions, are $\text{Fe}(\text{CO})_2\text{I}$ and the hitherto unknown iodide of univalent iron, FeI . $\text{Fe}(\text{CO})_2\text{I}_2$ is a reddish-brown solid; its alcoholic solution gives dark red $\text{Fe}(\text{CO})_2\text{I}_2$, phenan with *o*-phenanthroline, and green $\text{Fe}(\text{CO})_2\text{I}_2(\text{C}_5\text{H}_5\text{N})$ with pyridine. $\text{Fe}(\text{CO})_2\text{I}$ and FeI are extremely unstable; the latter is a bright red solid which reduces silver nitrate in acid

³⁰ A. Mittasch, *Z. angew. Chem.*, 1928, **41**, 827.

³¹ W. Manchot and J. König, *Ber.*, 1924, **57**, 2130.

³² W. Hieber and G. Bader, *Z. anorg. Chem.*, 1930, **190**, 193.

³³ W. Hieber and H. Lagally, *ibid.*, 1940, **245**, 295.

solution to metallic silver and reacts with water to form ferrous hydroxide and hydrogen. The molecular weights of these new compounds have not been determined, and the formulæ given are empirical.

Brief reference has been made above to a tricarbonyl halide of iridium of the type $\text{Ir}(\text{CO})_3\text{X}$; the other halides of this type have now been prepared and examined.³⁴ When dry carbon monoxide at atmospheric pressure is passed over the monohydrate of the iridium trihalide, $\text{IrX}_3 \cdot \text{H}_2\text{O}$, at about 150° , a mixture of $\text{Ir}(\text{CO})_3\text{X}$, $\text{Ir}(\text{CO})_2\text{X}_2$, and $[\text{Ir}(\text{CO})_3]_n$ sublimes on to the cooler parts of the apparatus. The dark brown, crystalline tricarbonyl halides sublime on heating the mixture at 115° , and the dicarbonyl compounds, which are colourless or yellow, sublime at 150° . Although the dicarbonyl halides are unstable and decompose on exposure to air, the tricarbonyl compounds are stable. It is interesting that halides of the type $\text{Ir}(\text{CO})_3\text{X}$ are not obtained from *anhydrous* iridium halides and carbon monoxide under the conditions described, although small yields of $\text{Ir}(\text{CO})_2\text{X}_2$ have been prepared from these reactants;³⁵ the necessity for the presence of water of hydration provides an interesting parallel to the use of methyl alcohol vapour as a catalyst in certain reactions in which carbonyl compounds are formed.³⁶ It is noteworthy that in the reaction just described iridium tricarbonyl is prepared, although in small yield, without the use of high-pressure technique. Hieber considers that formation of the iridium carbonyls, at both normal and high pressures, occurs by successive displacement of the halogen atoms in the halide by carbon monoxide.

Until recently, attempts to prepare carbonyls of the metals of Group VII (manganese, masurium, and rhenium) were unsuccessful, although the existence of well-defined carbonyl derivatives of Group VI and Group VIII metals led to a careful search for related compounds of the intervening Group VII elements, particularly manganese. The recent preparation of rhenium pentacarbonyl* halides³⁷ is therefore of special interest. These compounds, which have the formula $\text{Re}(\text{CO})_5\text{X}$, are prepared by heating a chloride of rhenium (ReCl_5 or ReCl_3), or potassium rhenibromide or rheniodide (K_2ReX_6) mixed with copper powder, in carbon monoxide at 200 atm. and $200\text{--}230^\circ$. Under these conditions the rhenium compounds are converted completely into the pentacarbonyl halide after about 30 hours; the pentacarbonyl derivatives are extracted from the products with benzene or light petroleum. The new compounds are stable, odourless, colourless or yellow crystalline solids which sublime unchanged in carbon monoxide but are decomposed on heating in air at about 400° . They are soluble in organic solvents but insoluble in water. The rhenium pentacarbonyl halides are similar in character and stability to the hexacarbonyls of the Group VI metals.

³⁴ W. Hieber, H. Lagally, and A. Mayr, *Z. anorg. Chem.*, 1941, **246**, 138.

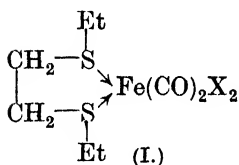
³⁵ W. Manchot and H. Gall, *Ber.*, 1925, **58**, 232.

³⁶ *E.g.*, in formation of $\text{Pd}(\text{CO})\text{Cl}$, W. Manchot and J. König, *ibid.*, 1926, **59**, 883.

³⁷ W. Hieber and H. Schulten, *Z. anorg. Chem.*, 1939, **243**, 164.

The unusual facility with which carbon monoxide reacts with certain metallic compounds containing sulphur directly bound to the metal atom has been noted above. This has led to a study of the chemistry of substituted carbonyls containing various groups attached to the metal atom by one or more atoms of sulphur; such compounds might occur as intermediates in the reactions in question. The tetracarbonyls of iron and cobalt react readily with ethyl- and phenyl-thiol to form stable, well-crystallised, red derivatives,^{37a, 38} $[\text{Fe}(\text{CO})_3\text{SEt}]_2$,³⁹ $[\text{Co}(\text{CO})_3\text{SEt}]_2$, $\text{Fe}(\text{CO})_3\text{SPh}$, and $\text{Co}(\text{CO})_3\text{SPh}$, with elimination of carbon monoxide and hydrogen. These are typical non-polar compounds. Diphenyl disulphide gives the same phenyl compound with iron tetracarbonyl, without elimination of hydrogen. Mercaptobenzthiazole in solution in light petroleum reacts with iron tetracarbonyl to give a red crystalline compound, $\text{Fe}_3(\text{CO})_{10} \begin{smallmatrix} \text{S} \\ \diagup \quad \diagdown \\ \text{S} \end{smallmatrix} \text{CH}_2$,

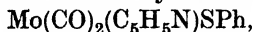
which is also formed in very small quantities from parathioformaldehyde, $(\text{CH}_2\text{S})_3$. α -Thionaphthol readily gives a dimeric compound analogous to $\text{Fe}(\text{CO})_3\text{SPh}$, but β -thionaphthol reacts with difficulty to form a derivative which is at least trimeric. Attempts to prepare chelate derivatives from iron tetracarbonyl and thiosemicarbazide, thiocatechol, thioacetamide, or



thiosalicylic acid were unsuccessful; a chelate iron carbonyl halide derivative (I) containing co-ordinated sulphur is, however, known.⁴⁰ Alkyl sulphides in light petroleum solution react with iron tetracarbonyl to form compounds of the type $\text{Fe}(\text{CO})_3\text{SR}_2$; some $\text{Fe}(\text{CO})_3\text{SR}$ is also formed, its amount increasing as the temperature is raised;

iron pentacarbonyl gives similar products. Dimethyl disulphide and the tetracarbonyl afford $[\text{Fe}(\text{CO})_3\text{SMe}]_2$, which is not conveniently prepared from the more volatile methyl sulphide. Amine-substituted carbonyls such as $\text{Fe}_2(\text{CO})_4(\text{C}_5\text{H}_5\text{N})_3$ with phenylthiol give $\text{Fe}(\text{CO})_3\text{SPh}$, but no amine-substituted derivatives of a similar type are formed; the compounds $\text{Fe}(\text{CO})\text{SPh}$, phenan and $\text{Co}(\text{CO})_2\text{SEt}$, phenan are formed, however, on treating $\text{Fe}(\text{CO})_3\text{SPh}$ and $[\text{Co}(\text{CO})_3\text{SEt}]_2$ with *o*-phenanthroline.

Nickel tetracarbonyl does not react with thiols. The hexacarbonyls of the Group VI metals do not react, but the substituted compound $\text{Mo}(\text{CO})_3(\text{C}_5\text{H}_5\text{N})_3$ gives a dark brown crystalline derivative,



showing that the partly substituted carbonyls may be more reactive than their parent compounds.³⁸

Little reference has been made above to the very numerous substituted carbonyls and carbonyl halides in which part of the carbon monoxide is replaced by amine, alcohol, or other groups; these are discussed in the

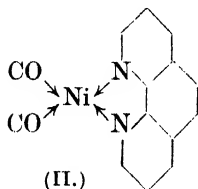
^{37a} W. Hieber and P. Spacu, *Z. anorg. Chem.*, 1937, **233**, 353.

³⁸ W. Hieber and C. Scharfenberg, *Ber.*, 1940, **73**, 1012.

³⁹ H. Reihlen, A. Gruhl, and G. von Hessling, *Annalen*, 1929, **472**, 268.

⁴⁰ W. Hieber, *Z. anorg. Chem.*, 1931, **201**, 329.

reviews cited ^{2, 3} and in the references given below.⁴¹ A few of these compounds, *e.g.*, the *o*-phenanthroline derivative (II) of nickel tetracarbonyl, can be formulated without difficulty as compounds in which the metal atom has the same electron configuration as in the parent carbonyl. Most of the substituted carbonyls, however, are more complex, and their structures deserve further study.



The "carbonyls" of the alkali metals have not been included, since there is no evidence that they are true carbonyls containing co-ordinated carbon monoxide molecules.

Closely related to the carbonyls are the volatile *nitrosyl carbonyls* of cobalt and iron, $\text{Co}(\text{CO})_3\text{NO}$ ⁴² and $\text{Fe}(\text{CO})_2(\text{NO})_2$,⁴³ which are the only compounds of their class so far discovered; both may be prepared by the reaction of nitric oxide with either of the corresponding polynuclear carbonyls under appropriate conditions. The cobalt compound is conveniently prepared by a method involving the cobalt cysteine complexes discussed above; carbon monoxide is passed into the alkaline cobalt salt solution containing cysteine, which is then acidified; on passing in nitric oxide the nitrosyl carbonyl is evolved as a red vapour.¹⁹ Cobalt nitrosyl carbonyl can also be obtained, in a similar manner, from an alkaline suspension of cobalt cyanide or sulphide in which carbon monoxide has been absorbed.²² A nitrosyl carbonyl of nickel has not yet been isolated, although a compound $\text{Ni}(\text{NO})_2\text{CO}$ might be expected to exist; the action of nitric oxide on nickel tetracarbonyl affords compounds of a univalent radical $\text{Ni}(\text{NO})$, *e.g.*, $\text{Ni}(\text{NO})\text{OH}$.⁴⁴

Reference has been made in the literature and in patents ⁴⁵ to a volatile cobalt nitrosyl, $\text{Co}(\text{NO})_3$, but the properties of this interesting compound have not been described. Non-volatile "nitrosyls" of iron, $\text{Fe}(\text{NO})_4$,⁴⁶ and ruthenium, $\text{Ru}(\text{NO})_4$ or $\text{Ru}(\text{NO})_5$,⁴⁷ have also been described, but the former is probably a hyponitrite, $\text{Fe}(\text{NO})_2\text{N}_2\text{O}_2$, and the latter requires further investigation to clarify its constitution.

An interesting new group of cobalt nitrosyl halides, $\text{Co}(\text{NO})_2\text{X}$, has

⁴¹ Work by W. Hieber and his collaborators: (iron compounds) *Ber.*, 1928, **61**, 558, 2421; *Sitzungsber. Heidelberg. Akad. Wiss., math.-nat. Kl.*, 1929, Part 3, 3-9; *Ber.*, 1930, **63**, 973; *Z. anorg. Chem.*, 1930, **190**, 193; *Ber.*, 1930, **63**, 1405; 1931, **64**, 2340; *Z. anorg. Chem.*, 1931, **201**, 329; *Ber.*, 1932, **65**, 1082; (nickel and cobalt compounds) *ibid.*, p. 1090; (chromium and molybdenum compounds) *Z. anorg. Chem.*, 1935, **221**, 337; (tungsten compounds) *ibid.*, p. 349.

⁴² R. L. Mond and A. E. Wallis, *J.*, 1922, **121**, 32.

⁴³ W. Hieber and J. S. Anderson, *Z. anorg. Chem.*, 1932, **208**, 238. For some reactions of the iron and cobalt nitrosyl carbonyls, see *idem, ibid.*, 1933, **211**, 132.

⁴⁴ J. S. Anderson, *ibid.*, 1936, **229**, 357; cf. also J. C. W. Frazer and W. E. Trout, *J. Amer. Chem. Soc.*, 1936, **58**, 2201.

⁴⁵ W. Hieber, *Angew. Chem.*, 1936, **49**, 463; I. G. Farbenindustrie A.-G., D.R.-P. 613,400, 613,401 (1932).

⁴⁶ W. Manchot and E. Enk, *Annalen*, 1929, **470**, 275.

⁴⁷ W. Manchot and W. J. Manchot, *Z. anorg. Chem.*, 1936, **226**, 410.

recently been described.⁴⁸ These compounds are prepared by the action of nitric oxide on the anhydrous cobalt halide at about 60°. The iodide is most readily prepared and forms dark brown or black, shining crystals. In the case of the bromide or chloride the reaction proceeds to completion only in presence of a metal, such as zinc or cobalt, which absorbs the halogen. An alcoholic solution of cobaltous iodide also reacts with nitric oxide, affording the dinitrosyl iodide. The cobalt dinitrosyl halides are extremely stable substances which can be sublimed without decomposition in air, carbon monoxide, or hydrogen at normal pressures; at high pressures carbon monoxide reacts to give cobalt tetracarbonyl and cobalt nitrosyl carbonyl. The compounds are regarded as true nitrosyl derivatives; they react readily with alkali thiosulphate solutions, giving deep green solutions of $[\text{Co}(\text{NO})_2(\text{S}_2\text{O}_3)_2]^{4-}$,⁴⁹ and also with alkali sulphide solutions; in the latter case compounds of the type $\text{Co}(\text{NO})_2\text{SM}$ (where M is a univalent metal), analogous to Roussin's red salts, are possibly formed. Organic amines give various additive and substitution products of the nitrosyl halides; pyridine gives $\text{Co}(\text{NO})\text{I} \cdot (\text{C}_5\text{H}_5\text{N})_6$, whereas *o*-phenanthroline does not displace nitric oxide, but forms $\text{Co}(\text{NO})_2\text{I} \cdot \text{phenan}$. The cobalt nitrosyl halides are clearly related to the carbonyl mercaptides described above, and also to the known compounds $\text{Fe}(\text{NO})_2\text{X}$,⁵⁰ $\text{Fe}(\text{NO})_2\text{SM}$ (Roussin's red salts), $\text{Fe}(\text{NO})_2\text{SR}$, $\text{Co}(\text{NO})_2\text{SR}$, $\text{Ni}(\text{NO})\text{SR}$, etc.⁵¹

Little attention has been paid above to the molecular constitution of the carbonyls and nitrosyls, since the general principles governing their structures have been adequately dealt with in these Reports¹ and in a recent review;⁵² this review also considers a number of nitrosyl cyanides which have not been included in this Report. Special importance attaches, however, to the examination by electron-diffraction and X-ray methods of the structures of iron pentacarbonyl,⁵³ the Group VI metal hexacarbonyls,⁵⁴ nickel tetracarbonyl, cobalt nitrosyl carbonyl, iron nitrosyl carbonyl,⁵⁵ iron enneacarbonyl $[\text{Fe}_2(\text{CO})_9]$,⁵⁶ and the cobalt and iron tetracarbonyl hydrides.⁵⁷ The structures of the carbonyl hydrides are of particular interest, since the hydrogen atoms are not attached directly to the metal atoms but to the carbonyl group, $\text{M}-\text{C}-\text{O}-\text{H}$ (the lines here do not indicate the character of

⁴⁸ W. Hieber and R. Marin, *Z. anorg. Chem.*, 1939, **240**, 241.

⁴⁹ W. Manchot *et al.*, *Ber.*, 1926, **59**, 2445; 1929, **62**, 681.

⁵⁰ W. Manchot and H. Fischer, *Diss.*, Tech. Hochschule, München, 1937. For other iron nitrosyl compounds, cf. ref. (51).

⁵¹ H. Reihlen *et al.*, *Annalen*, 1927, **457**, 71; 1928, **465**, 72; 1929, **472**, 268; 1930, **482**, 161; W. Manchot and F. Davidson, *Ber.*, 1929, **62**, 681.

⁵² A. A. Blanchard, *Chem. Reviews*, 1940, **26**, 409.

⁵³ R. V. G. Ewens and M. W. Lister, *Trans. Faraday Soc.*, 1939, **35**, 681; *Ann. Reports*, 1939, **36**, 166.

⁵⁴ L. O. Brockway, R. V. G. Ewens, and M. W. Lister, *Trans. Faraday Soc.*, 1938, **34**, 1350.

⁵⁵ L. O. Brockway and P. C. Cross, *J. Chem. Physics*, 1935, **3**, 828; L. O. Brockway and J. S. Anderson, *Trans. Faraday Soc.*, 1937, **33**, 1233.

⁵⁶ H. M. Powell and R. V. G. Ewens, *J.*, 1939, 286.

⁵⁷ R. V. G. Ewens and M. W. Lister, *Trans. Faraday Soc.*, 1939, **35**, 681.

the bonds). The hydrides may therefore be formulated as $\text{Co}(\text{CO})_3\text{COH}$ and $\text{Fe}(\text{CO})_2(\text{COH})_2$; the valency relation of the COH groups to the metal atoms appears to be analogous to that of the nitrosyl groups in the nitrosyl carbonyls.

A. J. E. W.

3. ISOTOPE EXCHANGE IN INORGANIC CHEMISTRY.

In recent years considerable use has been made of partly enriched non-radioactive isotope mixtures and also of radioactive isotopes in the elucidation of many of the problems of inorganic chemistry. Much of the work has been concerned primarily with problems of a more or less physical nature, but in many cases the bearing on inorganic chemistry has been considerable, and this is here reviewed.

Isotopic Concentration by Methods of Chemical Exchange.

Of the various methods available for the concentration of isotopes in their mixtures, those dependent on gaseous diffusion, fractional distillation, and fractional electrolysis have been extensively employed and are already widely known. The more recent application of thermal diffusion in gases and liquids to the separation of isotopic mixtures was reviewed in last year's Report.¹ However, apart from sections devoted to it in general reviews on methods of isotopic separation,² no account of the chemical exchange methods of separation has yet appeared.

That chemical exchange reactions could be employed in the practical separation of isotopes was first suggested by H. C. Urey and L. J. Grieff.³ The existence of equilibria in exchange reactions and the experimental verification that the constants of these equilibria can be evaluated by statistical methods, permit the evaluation from spectroscopic data of equilibrium constants and enrichment factors for possible exchange reactions. In the case of exchanges involving only one isotopic pair the enrichment factor is defined as $(N_1/N_2)/(n_1/n_2)$, where N_1 and N_2 are the numbers of light and of heavy atoms in the one compound, and n_1 and n_2 the corresponding numbers for the other. Provided that the assumption that the atoms distribute themselves statistically among the various molecules is made, and that the fundamental molecular constants for the two isotopic species are available, then the calculation of this enrichment factor can be made with reasonable accuracy. On the basis of their calculations, it was suggested by Urey and Grieff that isotopes of lighter elements might be separated by chemical exchange methods and that the equilibria might be established in liquid-gas two-phase systems by a counter-current operation. Theoretical calculations of the overall enrichment factors to be expected in scrubbing columns of a theoretical design were made. These calculations

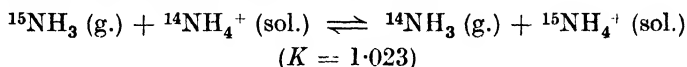
¹ P. 153.

² N. S. Bayliss and R. W. Pickering, *J. Proc. Austral. Chem. Inst.*, 1940, **7**, 51; H. C. Urey, *Rep. Prog. Physics*, 1939, **6**, 48.

³ *J. Amer. Chem. Soc.*, 1935, **57**, 321.

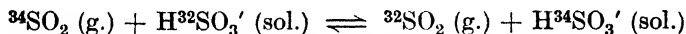
indicated that the process was favourable for enrichment of certain of the rare isotopes.

The practical application of this method involves the use of three distillation units in cascade ^{4,5} as had been suggested earlier by H. C. Urey, J. R. Huffman, H. G. Thode, and M. Fox.⁶ If each stage of the cascade increases the concentration by a factor β , then the first unit should have a flow β times that of the second, and the second a flow β times that of the third, the isotopic ratio being increased theoretically by a factor β^3 , whilst the total transport should be the same in each unit. The original distillation apparatus ⁵ consisted of three units with an effective column length of 115 feet, in sections some 15 feet long. Only the second and the third unit of this apparatus being used for the exchange reaction between gaseous ammonia and ammonium nitrate solution, *viz.*,



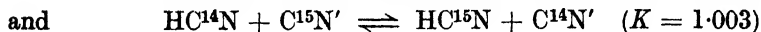
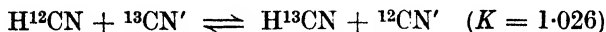
a 46-fold increase in the isotopic ratio $^{15}\text{N}/^{14}\text{N}$ was obtained in the solution in 2 weeks' operation, the sample containing 14.8% of ^{15}N .⁴ With all three units in operation, 8.8 g. of 70.6% ^{15}N were obtained in 4 days.⁵

The sulphur isotope ^{34}S has been obtained in 6.8% concentration in the liquid in 7 days, only one unit of the apparatus being used, for the exchange between gaseous sulphur dioxide and sodium bisulphate solution.⁴ Exchange has also been observed in the system $\text{H}_2\text{S} (\text{g.}) - \text{NaHS} (\text{sol.})$, the ^{34}S being concentrated in the gas phase.⁷ D. W. Stewart and K. Cohen ⁸ have found satisfactory exchange to take place between gaseous sulphur dioxide and an aqueous solution of sodium bisulphite according to the equation



The maximum concentration of ^{34}S was 27% after 21 days at a rate of 0.8 g. of ^{34}S per day.

Successful concentration of the heavy carbon isotope ^{13}C has also been accomplished by exchange between gaseous hydrogen cyanide and sodium cyanide solution by a similar method.^{9,10} The possible reactions involved are



The equilibrium constants quoted have been derived from the known vibrational frequencies of HCN and CN'. ^{15}N is concentrated to a small

⁴ H. G. Thode, J. E. Gorham, and H. C. Urey, *J. Chem. Physics*, 1938, **6**, 296.

⁵ H. G. Thode and H. C. Urey, *ibid.*, 1939, **7**, 34.

⁶ *Ibid.*, 1937, **5**, 856.

⁷ H. C. Urey, A. Mills, I. Roberts, H. G. Thode, and J. R. Huffman, *ibid.*, 1939, **7**, 138.

⁸ *Ibid.*, 1940, **8**, 905.

⁹ I. Roberts, H. G. Thode, and H. C. Urey, *ibid.*, 1939, **7**, 137.

¹⁰ C. A. Hutchison, D. W. Stewart, and H. C. Urey, *ibid.*, 1940, **8**, 532.

extent in the liquid phase, whereas ^{13}C is concentrated to a greater extent in the gas. The average production of ^{13}C was 0.150 g. (in sodium cyanide containing 23% of ^{13}C) per day.

Base exchange reactions of zeolites with the chlorides of potassium, lithium, and ammonium are the basis of a method of isotopic concentration of ^{41}K , ^7Li , and ^{15}N .¹¹ The concentration of these isotopes is made possible by the difference in binding of the two isotopic ions with water and with zeolite in each case. Changes of 25% in the abundance ratio $^7\text{Li}/^6\text{Li}$, and of 10% in $^{39}\text{K}/^{41}\text{K}$ and $^{14}\text{N}/^{15}\text{N}$ were observed.

Exchange Reactions involving Non-radioactive Isotopes.—Exchange reactions occurring with non-radioactive isotopes have been investigated exhaustively in the cases of deuterium and to a less extent of the heavy oxygen isotope ^{18}O and the heavy nitrogen isotope ^{15}N . A very comprehensive account of the exchange reactions involving deuterium has been given by H. C. Urey and G. K. Teal,¹² and they will not be further discussed here.

Oxygen exchange. Interchange of ^{18}O from heavy-oxygen water with sulphate ions was reported by S. C. Datta, J. N. E. Day, and C. K. Ingold¹³ to be very slow in neutral solution at 100°, whereas in alkaline solution rapid interchange was found at the same temperature. These workers postulated a mechanism for the exchange, assuming the active agent to be the hydroxide ion $^{18}\text{OH}'$. However, subsequent investigations by E. R. S. Winter, (Miss) M. Carlton, and H. V. A. Briscoe¹⁴ have shown that heavy-oxygen water, having an excess density due to ^{18}O of 150–200 γd , does not interchange with sulphate in neutral, acid, or alkaline solution at 100°. It was suggested that the interchange observed by Ingold *et al.* was actually an interchange with silicate ions produced by alkali attack upon the glass container. T. Titani and K. Goto¹⁵ reported partial exchange of potassium bisulphate with H_2^{18}O and this has been confirmed by G. A. Mills,¹⁶ who suggests that the mechanism responsible for the exchange is one of reversible anhydride formation, $\text{H}_2\text{SO}_4 \rightleftharpoons \text{H}_2\text{O} + \text{SO}_3$, a reaction favoured by acidic conditions. A further investigation¹⁷ confirms that no exchange occurs between H_2^{18}O and sulphate in neutral or alkaline solution, but that hydrogen chloride catalyses the exchange. The latter result is in good agreement with Titani and Goto, but not with Briscoe *et al.*, who used sulphuric acid. Furthermore, J. L. Hyde¹⁸ has recently published results which indicate that the H_2^{18}O exchange with sulphate ions is catalysed by H^+ but not by OH' . No exchange was observed in neutral solution. It appears that the most satisfactory mechanism is one of reversible anhydride formation in acid solutions, as was suggested by Mills.

¹¹ T. I. Taylor and H. C. Urey, *J. Chem. Physics*, 1938, **6**, 429.

¹² *Rev. Mod. Physics*, 1935, **7**, 34.

¹³ *J.*, 1937, 1968.

¹⁴ *J.*, 1940, 131.

¹⁵ *Bull. Chem. Soc. Japan*, 1939, **14**, 77.

¹⁶ *J. Amer. Chem. Soc.*, 1940, **62**, 2833.

¹⁷ N. F. Hall and O. R. Alexander, *ibid.*, p. 3455.

¹⁸ *Ibid.*, 1941, **63**, 873.

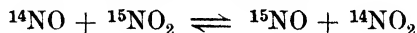
A similar situation obtains in the case of phosphate, where a base catalysis has been reported by E. Blumenthal and J. B. M. Herbert¹⁹ and T. Titani, N. Morita, and K. Goto,²⁰ but could not be repeated when steps were taken to eliminate the possibility of alkali attack on the glass containers.¹⁴

Chlorate and nitrate have been found by Briscoe *et al.*¹⁴ to interchange completely in acid solution, but not in neutral or alkaline solution, although other workers¹⁷ find that addition of acid has little influence on the non-exchange in nitrate.

Rapid and complete exchange in neutral solution has been observed in the case of SiO_3'' , BO_2' , BO_3''' , $\text{B}_4\text{O}_7''$, $\text{Cr}_2\text{O}_7''$, CrO_4'' , MoO_4'' , WO_4'' , CO_3'' , MnO_4' , IO_3' , SeO_3'' , SO_3'' , $\text{S}_2\text{O}_3''$, AsO_4''' , and AsO_2' , but not with NO_2' , ClO_4' , ClO_3' , and SeO_4'' .^{14, 16, 17} It is possible that the exchange may take place in one of three ways: (i) Direct interchange of oxygen atoms. (ii) Addition, and subsequent removal, of water or hydroxyl ion to the anion with possible exchange. (iii) Formation of undissociated acid by hydrolysis, followed by reversible anhydride formation, as has already been formulated in the case of sulphate exchange. The experimental data appear to be adequately explained by the last of these possibilities, for in all cases the rate of ^{18}O exchange is related to the acid strength of the corresponding acid.¹⁶

Isotope exchange between gaseous oxygen and water vapour on catalytic oxide surfaces has been reported by N. Morita.²¹ For aluminium oxide surfaces, it was found that the rate of exchange is almost independent of the composition of the gas mixture, indicating that the determining factor is the activated adsorption of water on the oxide surface. The activation energy of this exchange is calculated to be 18–20 kg.-cals.

Nitrogen exchange. The exchange of ^{15}N between nitrogen di- and mon-oxide in the gas phase has given a very interesting confirmation of the structure of the dinitrogen trioxide molecule, which is known to occur in these mixtures.²² The exchange reaction, *viz.*,



was found to be rapid and only the lower limit of the exchange rate could be established. Assuming the intermediate formation of N_2O_3 , the existence of which has been demonstrated by measurements of the equilibrium constant and by absorption-spectra data, the mere fact of exchange requires an oxygen bridge in the N_2O_3 molecule, such as $\text{O}=\text{N}-\text{O}-\text{N}=\text{O}$. This structure is to be expected on account of the symmetry of the resonance state.

Several recent investigations have been directed at the possibility of exchange between gaseous and combined nitrogen, in an endeavour to elucidate the mechanism of nitrogen fixation by plants. Exchange was reported to occur between gaseous nitrogen containing radioactive ^{15}N and

¹⁹ *Trans. Faraday Soc.*, 1937, **33**, 849. ²⁰ *Bull. Chem. Soc. Japan*, 1938, **13**, 329.

²¹ *Ibid.*, 1940, **15**, 47, 298.

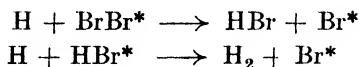
²² E. Leifer, *J. Chem. Physics*, 1940, **8**, 301.

solutions of sodium nitrite, sodium nitrate, hydroxylamine hydrochloride, and sodium hexanitrocobaltate(III) by Y. Nishina, T. Imori, H. Kuto, and H. Nakayama,²³ but other workers, using heavy nitrogen gas (¹⁵N)^{24, 25} and radioactive nitrogen gas (¹³N),²⁶ failed to observe any exchange with combined nitrogen in solution. It appears, therefore, that the fixation of nitrogen in plants does not occur by direct exchange of gaseous and combined nitrogen.

The adsorption and nitrogen isotope exchange on iron, tungsten, and osmium catalytic surfaces have been investigated recently by H. S. Taylor and his co-workers.^{27, 28} The exchange may be represented thus: $^{28}\text{N}_2 + ^{30}\text{N}_2 \rightleftharpoons 2^{28}\text{N}^{30}\text{N}$ and appears to be of the second order. Small quantities of hydrogen were found to inhibit the exchange on osmium, and large amounts to suppress it, whereas on iron surfaces the presence of hydrogen accelerated the exchange. This exchange process apparently requires migration of atoms to positions favourable to exchange; in the case of osmium, the adsorbed hydrogen (where the adsorption is some 15 times greater than that of nitrogen) impedes this migration. The fact that the activation energy of exchange is 50 kg.-cals. for iron and 22 kg.-cals. for osmium surfaces indicates a greater lability of nitrogen on the osmium surface and a weaker Os-N than Fe-N bond. This is in agreement with the stability of the known iron nitrides and the non-existence of analogous osmium compounds.

Exchange Reactions involving Radioactive Isotopes.—Exchange reactions between radioactive isotopes and inorganic compounds have been recently discussed in an excellent and comprehensive review on artificial radioactivity by G. T. Seaborg.²⁹ This section will be entirely supplementary to Seaborg's article, indicating only those radioactive exchanges of inorganic interest which have been investigated in the last two years.

L. C. Liberatore and E. O. Wiig³⁰ have made a study of the exchange of radioactive bromine (produced by the bombardment of selenium with protons) with hydrogen bromide in the gas phase. Calculations indicate that the postulate of an intermediate cluster of molecules would lead to an exchange rate some 10^{12} times too small, whereas a chain mechanism leads to a rate of the same order as that determined experimentally. Free bromine atoms are produced by the reactions (where Br* indicates a radioactive bromine atom)



²³ *J. Chem. Physics*, 1941, **9**, 571.

²⁴ R. H. Burris and C. E. Miller, *Science*, 1941, **93**, 114.

²⁵ G. G. Joris, *J. Chem. Physics*, 1941, **9**, 775.

²⁶ T. H. Norris, S. Ruben, and M. D. Kamen, *ibid.*, p. 726.

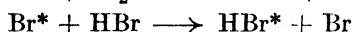
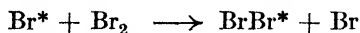
²⁷ G. G. Joris and H. S. Taylor, *ibid.*, 1939, **7**, 893.

²⁸ W. R. F. Guyer, G. G. Joris, and H. S. Taylor, *ibid.*, 1941, **9**, 287.

²⁹ *Chem. Reviews*, 1940, **27**, 199.

³⁰ *J. Chem. Physics*, 1940, **8**, 165.

after which equilibrium is attained by the partition of the Br^* between molecular bromine and hydrogen bromide :

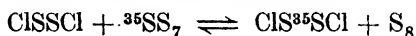


W. F. Libby,³¹ however, on the basis of exchange carried out at reduced radioactive concentrations, suggests that the alternative bimolecular mechanism of intermediate formation of HBr_3 is correct. Liberatore and Wiig in a further publication³² report no exchange of radioactive bromine with gaseous ethyl bromide at room temperature, but on heating to 200—300° rapid exchange was found to set in. The fact that the $\text{Cl}-\text{Br}$ bond is weaker than the $\text{H}-\text{Br}$ bond would require exchange of bromine with ethyl bromide also to occur at room temperature if Libby's mechanism were correct. The atomic exchange mechanism requires activation energies of 25 and <5 kg.-cals. for ethyl bromide and hydrogen bromide, respectively, the latter exchange therefore being the only one which can proceed at room temperature. This is in accordance with the experimental results.

Phosphoric acid containing radioactive ^{32}P (half-life 14.3 days), in solution with disodium hydrogen phosphate, has been used as an end-point indicator in the volumetric estimation of cations which form insoluble phosphates, *e.g.*, Mg^{++} , Ag^+ , Ba^{++} , Pb^{++} , Th^{++++} , and UO_2^{++} .³³

It has been shown that no exchange of radioactive ^{32}P occurs between ortho-, pyro-, and meta-phosphoric acids in acid or alkaline solutions.³⁴ Furthermore, by using ^{32}P as an indicator, the completeness of separation of meta- from other phosphoric acids by precipitation with barium ions has been demonstrated, whereas in the precipitation of pyrophosphate with Cd^{++} a small amount of co-precipitation of ortho-phosphate occurs.

Elementary radioactive sulphur (^{35}S) has been shown³⁵ to exchange with sulphur monochloride according to the reaction



the rate of exchange being directly proportional to the concentration of S_8 molecules. The most satisfactory mechanism involves a slow stage $\text{S}_8 \rightleftharpoons \text{S}_6 + \text{S}_2$, followed by a rapid stage $\text{S}_2 + \text{S}_2\text{Cl}_4 \rightleftharpoons 2\text{S}_2\text{Cl}_2$.

Applications to the Chemistry of Complex Compounds.—Several recent investigations have demonstrated the usefulness of isotopic exchange reactions in solving problems associated with the chemistry of co-ordination complexes. Up to the present, only radioactive exchange has been employed in this field, but with obvious success. A. A. Grünberg and P. M. Filinov³⁶ have used radioactive bromine to demonstrate the free exchange between the complex anions, tetrabromoplatinate(II), $[\text{PtBr}_4]^{--}$, and hexabromoplatinate(IV), $[\text{PtBr}_6]^{--}$, (containing radiobromine) and

³¹ *J. Chem. Physics*, 1940, **8**, 348.

³² *Ibid.*, p. 349.

³³ A. Langer, *J. Physical Chem.*, 1941, **45**, 639.

³⁴ D. E. Hull, *J. Amer. Chem. Soc.*, 1941, **63**, 1269.

³⁵ R. A. Cooley and D. M. Yost, *ibid.*, 1940, **62**, 2474.

³⁶ *Compt. rend. Acad. Sci. U.R.S.S.*, 1939, **23**, 912.

bromine ions in solution. This work has been extended by A. A. Grünberg.³⁷ Confirmation of the existence of an equilibrium between Br' and the above platinum complexes was obtained, as the exchange can take place only if the complex dissociates with subsequent recombination. The functional equivalence of the bromine atoms in the complex anions was demonstrated by the equilibrium



Interchange between the complexes themselves has also been established in the two following observed exchanges :

- (i) $K_2[PtBr_4] + cis-[Pt(NH_3)_2Br_2^*] \rightleftharpoons K_2[PtBr_2^*Br_2] + [Pt(NH_3)_2Br_2]$
- (ii) $K_2[PtBr_4] + K_2[PtBr_6^*] \rightleftharpoons K_2[PtBr_4^*] + K_2[PtBr_2^*Br_2]$

but, on using the radioactive isotopes of platinum and iridium, no exchange was found to occur between stable complexes such as $K_2[PtCl_6]$ and $[Pt(NH_3)_2Cl_4]$; $(NH_4)_2[IrCl_6]$ and $[Ir py_2 Cl_4]$; $(NH_4)_3[IrCl_6]$ and $H[Ir py_2 Cl_4]$.

Cobalt(III) in certain complex compounds has been found not to exchange with radioactive Co^{++} ions in solution³⁸ according to the expected reaction $Co^{++} \rightleftharpoons Co^{+++}$. The only stable forms of cobalt(III) occur in cobalt complexes, and in aqueous solutions of these a small concentration of Co^{+++} in equilibrium with the complexes is to be expected. However, exchange could only be observed if (i) the exchange $Co^{++} \rightleftharpoons Co^{+++}$ were operative, and (ii) the exchange were more rapid than the reduction of Co^{+++} by water. As exchange due to electron transfer is very probable, then the failure to observe it may be due to decomposition by reduction before measurable exchange can occur.

F. A. Long³⁹ has studied the exchange of oxalate ions with the tri-oxalato-compounds of the tervalent metals cobalt, iron, aluminium, and chromium (containing the radioactive ^{14}C isotope). Exchange was found to occur with potassium trioxalato-ferrate(III) and -aluminate(III), $K_3[M(C_2O_4)_3]$, but not with the analogous chromium and cobalt compounds. Theoretical considerations indicate that the bonds in various co-ordination complexes can approach either covalent or ionic types fairly closely. Where strong *s-p-d* hybridisation occurs covalent bonding is expected, as is indicated in the case of the cobalt and chromium complexes by the values of their magnetic susceptibilities.⁴⁰ With aluminium compounds, however, *s-p-d* hybridisation is improbable, and in the case of the iron complexes, analogous complexes have been shown to possess bonds of the ionic type. Furthermore, the most recent work⁴⁰ indicates that Fe(III) and Al(III) complexes are not capable of resolution into optical isomers, and this should be possible if the oxalate-central atom bonds were of the ionic rather than the covalent type. The resolution of Co(III) and Cr(III) complexes is a well-established fact, indicating covalent bond types. This is in complete

³⁷ *Bull. Acad. Sci. U.R.S.S., Sér. Phys.*, 1940, **4**, 342.

³⁸ J. F. Flagg, *J. Amer. Chem. Soc.*, 1941, **63**, 557.

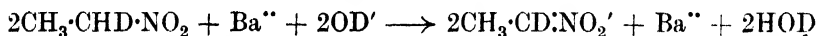
³⁹ *Ibid.*, 1939, **61**, 570; 1941, **63**, 1353.

⁴⁰ C. H. Johnson, *Trans. Faraday Soc.*, 1932, **28**, 845.

agreement with the exchange measurements, where exchange is expected only in those complexes involving ionic bond types, such as those of Fe(III) and Al(III), but not those of Cr(III) and Co(III).

Exchange has been found to occur between mercuric iodide and ammonium iodide (containing radioactive iodine) when the complex $(\text{NH}_4)_2\text{HgI}_4$ is formed and subsequently decomposed. Similar results have been obtained in the reactions of ammonium iodide with bismuth iodide and lead iodide through the intermediate formation of the complex anions $[\text{BiI}_4]'$ and $[\text{PbI}_4]''$, suggesting that no essential difference exists between normal and co-ordinate covalencies in these complexes.⁴¹

Although the isotope effect in band spectra of molecules has been well known for many years, only one case is on record where the visual colour or light absorption of a compound has been affected to a large extent by isotopic substitution. S. H. Maron and V. K. LaMer⁴² have reported a change in the colour of the $\text{CH}_3\cdot\text{CH}\cdot\text{NO}_2'$ ion on substitution of the α -hydrogen atom by a deuterium atom. The addition of barium deuterioxide, $\text{Ba}(\text{OD})_2$, to nitroethane in heavy water yields the colourless ion $\text{CH}_3\cdot\text{CHD}\cdot\text{NO}_2'$, which, on addition of D_2SO_4 , yields the compound $\text{CH}_3\cdot\text{CHD}\cdot\text{NO}_2$. Addition of $\text{Ba}(\text{OD})_2$ to this produces a light yellow colour due to the formation of the ion $\text{CH}_3\cdot\text{CD}\cdot\text{NO}_2'$, according to the reaction



Absorption-spectra measurements of solutions containing this ion show an absorption starting in the region $\lambda\lambda$ 5000—5200 Å. and continuing into the ultra-violet. It is possible that similar differences in colour may be found later in inorganic isotopic pairs.

A. L. G. R.

H. J. EMELÉUS.

A. L. G. REES.

A. J. E. WELCH.

⁴¹ S. Chatterjee and P. Rây, *J. Indian Chem. Soc.*, 1940, **17**, 524.

⁴² *J. Chem. Physics*, 1938, **6**, 299.

CRYSTALLOGRAPHY.

1. INTRODUCTION.

THIS Report is divided into four main sections, dealing with the more physical aspects of crystallography (2), metal structures (3), inorganic structures (4), and organic structures (5). Space does not permit a very full treatment of all these subjects, and in some cases it has been necessary to confine the account to certain special topics only. Attention should be drawn, however, to a number of general articles which have recently appeared dealing with various aspects of X-ray technique, including the determination of equilibrium diagrams,¹ the accurate determination of lattice spacings,² the construction of powder cameras,³ photometry,⁴ and related subjects.

In last year's Report we referred briefly to the subject of "diffuse" reflections from crystals, which are additional to the normal Laue pattern, and can be obtained with monochromatic X-rays. A very large amount of new literature on this subject has been published during the year, and this is reviewed in Section 2. At first sight, and taken as a whole, the effect of these new contributions may be to confuse rather than to clarify. Nevertheless, the experimental study of the subject is now much more complete, and it is clear that the extra, non-Laue reflections may have more than one origin. Some of these reflections are "structure sensitive": they depend on the history and treatment of the particular crystal specimen, vary but little with temperature, and are no doubt associated with some kind of internal strain. On the other hand, we have the true "temperature sensitive" diffuse spots, which are greatly enhanced at high temperatures and disappear at low temperatures. The balance of the evidence appears to indicate that the latter are due to elastic thermal vibrations in the crystal, which give rise to new regularities in the density distribution, and hence to new crystal reflections at high temperatures.

In the field of metal and alloy structures (Section 3) relatively few new types have been discovered in recent years. There have been many improvements in technique, however, and details of some of the earlier structures can now be more accurately defined. A notable example of such work is the precise location of the carbon atoms in cementite, Fe_3C . Another important field which is now being actively pursued lies in the study of intermediate structures during transformations in the solid state, such as the nature of the precipitation of copper in an alloy of copper and aluminium. Another interesting study of structural imperfections of another sort has been carried out in the case of cobalt, and an explanation of the existence

¹ A. J. Bradley, (Sir) W. L. Bragg, C. Sykes, *J. Iron Steel Inst.*, 1940, **141**, 63.

² H. Lipson and A. J. C. Wilson, *J. Sci. Instr.*, 1941, **18**, 144.

³ A. J. Bradley, H. Lipson, and N. J. Petch, *ibid.*, p. 216.

⁴ J. M. Robertson, R. H. V. M. Dawton, and A. H. Jay, *ibid.*, pp. 126, 128.

of sharp and "fuzzy" diffraction lines in the X-ray photographs has been given.

A large amount of new data has been obtained from the general inorganic structures (Section 4) and this includes many new values for interatomic distances, by both X-ray and electron-diffraction methods. A few general papers have been published, and a rather drastic revision of covalent single bond radii for F, O, and N has been proposed. One feels that the new values should be treated with some reserve until the numerous structures which involve their use have been further studied by the most accurate methods. Some further interesting results have been obtained during the year among structures containing complex ions, and these include data bearing on the constitution of the ferrocyanides. From the niobates further information has been obtained on the nature of the 7-co-ordinated complex, with the analysis of two almost equally stable types.

Very few complete investigations have been made for organic structures during the year, and this field is reviewed briefly in Section 5. The nature of the intramolecular fold in α -keratin and α -myosin has been discussed at length, and the result promises to be fundamental in protein structure, not only for the fibrous proteins, but for the corpuscular or globular proteins as well. It remains to be seen whether more detailed analysis of existing data, when that becomes possible, will bear out and refine the new ideas.

J. M. R.

2. TEMPERATURE EFFECTS IN THE REFLECTION OF X-RAYS FROM CRYSTALS.

The Report for 1940¹ described preliminary experimental and theoretical work on the "diffuse" reflections found on well-exposed Laue photographs of many crystalline substances. The year 1941 has greatly increased the literature on this subject, notably by means of a Discussion in the *Proceedings of the Royal Society*,²⁻¹¹ by a series of papers in the *Proceedings of the Indian Academy of Sciences*,¹²⁻¹⁵ and in the *Physical Review*,¹⁶⁻²⁴ and by articles and letters in *Nature*.²⁵⁻³⁴

¹ *Ann. Reports*, 1940, **37**, 167.

² G. D. Preston, *Proc. Roy. Soc.*, 1941, **A**, **179**, 1 (cf. 1939, **A**, **172**, 116).

³ (Mrs.) K. Lonsdale and H. Smith, *ibid.*, 1941, **A**, **179**, 8 [28 Plates].

⁴ (Sir) W. H. Bragg, *ibid.*, pp. 51, 94. ⁵ (Sir) W. L. Bragg, *ibid.*, p. 61.

⁶ C. G. Darwin, *ibid.*, p. 65. ⁷ G. I. Finch, *ibid.*, p. 67.

⁸ M. Born and (Miss) K. Sarginson, *ibid.*, p. 69.

⁹ (Sir) C. V. Raman, *ibid.*, pp. 289, 302.

¹⁰ (Mrs.) K. Lonsdale, *ibid.*, p. 315. ¹¹ H. A. Jahn, *ibid.*, p. 320.

¹² (Sir) C. V. Raman and P. Nilakantan, *Proc. Indian Acad. Sci.*, 1940, **11**, **A**, 379, 389, 398; **12**, **A**, 141.

¹³ (Sir) C. V. Raman and N. S. Nagendra Nath, *ibid.*, **12**, **A**, 83, 427.

¹⁴ (Sir) C. V. Raman, *ibid.*, 1941, **13**, **A**, 1.

¹⁵ S. Bhagavantam and J. Bhimasenachar, *ibid.*, 1940, **12**, **A**, 337; 1941, **13**, **A**, 266.

¹⁶ G. E. M. Jauncey and O. J. Baltzer, *Physical Rev.*, 1940, **58**, 1116; 1941, **59**, 699.

¹⁷ G. E. M. Jauncey, *ibid.*, p. 456.

¹⁸ G. E. M. Jauncey, O. J. Baltzer, and D. C. Miller, *ibid.*, p. 908.

The earliest example of diffuse reflection (by white radiation) is to be found on Laue photographs taken by Friedrich in 1913; this was correctly interpreted as a temperature effect by H. Faxén in 1923.³⁵ A more complete mathematical treatment of the effect of thermal vibrations in crystals generally upon the interference of X-rays was given, in terms of the earlier quantum mechanics, by I. Waller in 1925.³⁶ Other mathematicians^{37, 38, 8} have verified Waller's formulæ by means of a more rigorous quantum-mechanical deduction. The first deliberate experimental test of this theory, which indicates that the diffuse reflection depends upon the crystal orientation and thus conflicts with the better-known Debye theory, was made by J. Laval,³⁹ who, using ionisation spectrometer methods and monochromatised Cu and Mo radiation, showed that the general predictions of the Waller theory were essentially correct for the crystals examined (potassium and sodium chlorides, aluminium, calcite, diamond, and a powdered specimen of silver, the first over a temperature range of 289° to 665° K.). Preston^{2, 29} independently made similar observations by photographic methods; but his suggestion that the results could be interpreted by the assumption of small groups of atoms scattering independently of neighbouring groups, although receiving considerable early support,^{4, 6, 16, 17, 25, 28} was also adversely criticised.^{5, 19, 32, 33}

(Sir) C. V. Raman and his collaborators, who put forward an entirely different theory, *viz.*, that the X-rays excite the characteristic lattice vibrations and are reflected with a very small change of frequency by the new stratifications of density thus set up,^{12, 13, 14, 26, 27, 40} have published some excellent diffuse spot photographs of sodium nitrate, calcium carbonate, and sodium chloride; and have shown that in the first case a big temperature effect exists which varies for the different crystal planes. A somewhat different derivation of the thermal theory has been given by Zachariasen¹⁹ and it has been shown that the various reported results for potassium and sodium chlorides^{12, 16, 20} are in quantitative agreement with

¹⁹ W. H. Zachariasen, *Physical Rev.*, 1941, **59**, 207, 766, 860, 909.

²⁰ S. Siegel, *ibid.*, p. 371; R. Q. Gregg and N. S. Gingrich, *ibid.*, p. 619.

²¹ P. Kirkpatrick, *ibid.*, p. 452.

²² O. J. Baltzer, *ibid.*, 1941, **60**, 460.

²³ (Sir) C. V. Raman and P. Nilakantan, *ibid.*, p. 63.

²⁴ (Mrs.) K. Lonsdale and H. Smith, *ibid.*, p. 617.

²⁵ (Sir) W. H. Bragg, *Nature*, 1940, **146**, 509; 1941, **148**, 112.

²⁶ (Sir) C. V. Raman and P. Nilakantan, *ibid.*, 1940, **146**, 523, 686; 1941, **147**, 118.

²⁷ (Sir) C. V. Raman, P. Nilakantan, and P. Rama Pisharoty, *ibid.*, p. 805.

²⁸ G. E. M. Jauncey, *ibid.*, p. 146.

²⁹ G. D. Preston, *ibid.*, pp. 358, 467.

³⁰ (Mrs.) K. Lonsdale, *ibid.*, 1940, **146**, 806; 1941, **147**, 481.

³¹ H. A. Jahn and (Mrs.) K. Lonsdale, *ibid.*, p. 88.

³² M. Born, *ibid.*, p. 674.

³³ H. A. Jahn, *ibid.*, p. 511.

³⁴ (Mrs.) K. Lonsdale and H. Smith, *ibid.*, 1941, **148**, 112, 257, 628.

³⁵ *Z. Physik*, 1923, **17**, 266.

³⁶ Diss., Uppsala, 1925.

³⁷ M. v. Laue, *Ann. Physik*, 1926, **81**, 877; *Z. Krist.*, 1927, **65**, 493.

³⁸ H. Ott, *Ann. Physik*, 1935, **23**, 169.

³⁹ *Compt. rend.*, 1938, **207**, 169; 1939, **208**, 1512; *Bull. Soc. franç. Min.*, 1939, **62**, 137; C. Mauguin and J. Laval, *Compt. rend.*, 1939, **208**, 1446.

⁴⁰ (Sir) C. V. Raman and P. Nilakantan, *Current Sci.*, 1940, **9**, 165.

his formulæ, which, like those of Faxén and Waller, take account of the elastic constants of the crystal, since these influence the frequencies and amplitudes of the elastic (thermal) vibrations. Raman^{9,14} and Nilakantan²³ claim, however, that their results for diamond provide the most rigorous proof that it is the optical (characteristic) frequencies and *not* the acoustical (elastic) frequencies which are chiefly instrumental in giving the extra non-Laue reflections. Lonsdale and Smith, who have contributed a wide experimental survey of the geometrical and physical conditions governing the appearance of diffuse reflections for crystals of organic and inorganic compounds,³ have shown that diamond is very far from being either an ideal or a typical crystal.^{10, 24, 32} The relatively sharp anomalous reflections from diamond, to which Raman and Nilakantan first called attention, are in fact due to some structure-sensitive cause. They are given in varying intensity by normal diamonds, but are completely absent from photographs of the (more perfect?) diamonds classed as type II.⁴¹ They are only slightly, if at all, temperature-sensitive. All diamonds show the diffuse "temperature" spots predicted by the thermal theory; these are greatly enhanced at sufficiently high temperatures and disappear at low temperatures, thus conforming to the usual behaviour of such diffuse reflections.

The most reasonable conclusion appears to be that the structure-sensitive reflections found for normal diamonds are associated with some kind of internal strain. Lonsdale and Smith have pointed out^{3, 24} that cleaved or fractured crystals frequently give non-Laue reflections which are quite different in quality from the true diffuse reflections; and Kirkpatrick²¹ has reported an increase in anomalous reflecting power of cleaved calcite surfaces, when ground, which is undoubtedly due to the presence of very small disordered crystal particles.

It is clear, therefore, that care must be taken to distinguish between anomalous, structure-sensitive reflections due to crystal strains, whether intrinsic or externally applied, and those diffuse reflections which are temperature-sensitive and due to crystal vibrations. Jahn³³ has pointed out that if the extension of reflecting power about the normal (Bragg) reflecting positions is due to the finiteness of the reflecting crystal particles, the distribution will be essentially similar for different planes,⁴² whereas the distribution of diffuse reflecting power due to the existence of elastic vibrations will be different for different planes; and he has illustrated the variations to be expected in the latter case by application of the Waller formula to sodium single crystals,^{11, 33} which are soft and elastically very anisotropic. An experimental investigation of sodium and lithium single crystals³⁴ has shown that the observable diffuse reflections, which are detailed, intense, and persistent, are in entire agreement with the pre-

⁴¹ (Sir) R. Robertson, J. J. Fox, and A. E. Martin, *Phil. Trans.*, 1934, A, **232**, 463; *Proc. Roy. Soc.*, 1936, A, **157**, 579.

⁴² M. v. Laue, *Ann. Physik*, 1936, **26**, 55; M. v. Laue and K. H. Riewe, *Z. Krist.*, 1936, **95**, 408; P. P. Ewald, *Proc. Physical Soc.*, 1940, **52**, 167.

dictions of the elastic vibration (thermal) theory, as interpreted by Jahn. The fact that these monatomic cubic crystals, for which no optical vibrations are known,⁴³ do show diffuse reflections at all, is a strong indication that the observed effects are due to the elastic thermal atomic vibrations. The fact that "layer" and "chain" type structures each give typical and easily-recognisable diffuse photographs has already proved to be of assistance in crystal-structure determination.^{44, 3} If, as has been suggested, these diffuse patterns can in time be used to determine the elastic properties of single crystals at various temperatures, then it is clear that a new and useful field of research is being opened up.

K. L.

3. METAL STRUCTURES.

It is perhaps natural that the rate of discovery of new alloy structures should now tend to diminish. In the first place, it is probable that all the simple types of structure are known, so that any left are those whose determinations require much more time and patience. In the second place, interest in complicated structures is less, since they cannot be expected to produce any important modification of the general rules for the occurrence of the commoner structures such as the "electron compounds" (W. Hume-Rothery),¹ the "interstitial compounds" (G. Hägg),² and the "AB₂ compounds" (G. E. R. Schulze).³ Of the structures determined in about the last two years only three—CuMg₂,⁴ Au₄Al,⁵ and CaZn₅⁶—seem to be new; others, such as V₃Si⁷ and Li₁₀Pb₃,⁸ are similar to established structures.

There is evident, however, a tendency to go over the ground of earlier work in order to clear up problems left unsolved. Cementite, Fe₃C, is an example of this. The detection of the carbon atoms by X-rays had previously been considered almost impossible, but with accurate photometry and the use of three-dimensional Fourier series, H. Lipson and N. J. Petch⁹ have shown that they can be located unequivocally. Petch¹⁰ has also been able to detect the carbon atoms in austenite, the face-centred cubic solid solution of carbon in iron.

Improvements in technique have also shown that there are still problems associated with structures previously considered well established. H. Lipson and A. R. Stokes¹¹ have found that thallium has a body-centred cubic

⁴³ S. Bhagavantam, *Proc. Indian Acad. Sci.*, 1941, **13**, A, 543.

⁴⁴ (Mrs.) K. Lonsdale, *Proc. Roy. Soc.*, 1941, A, **177**, 272; (Mrs.) K. Lonsdale, J. M. Robertson, and (Miss) I. Woodward, *ibid.*, 1941, A, **178**, 43.

¹ "The Metallic State," 1931, p. 328, Oxford.

² *Z. physikal. Chem.*, 1931, B, **12**, 33. ³ *Z. Elektrochem.*, 1939, **45**, 849.

⁴ G. Ekwall and A. Westgren, *Arkiv Kemi, Min. Geol.*, 1940, **14**, B, 7.

⁵ O. E. Ullner, *ibid.*, 1940, **14**, A, 3.

⁶ W. Haucke, *Z. anorg. Chem.*, 1940, **244**, 17.

⁷ H. J. Wallbaum, *Z. Metallk.*, 1939, **31**, 362.

⁸ M. Alberto and E. Arregghini, *Z. Krist.*, 1939, **101**, 470.

⁹ *J. Iron Steel Inst.*, 1940, **142**, 95.

¹⁰ *Ibid.* (in press).

¹¹ *Nature*, 1941, **148**, 437.

structure at 262° , although it is commonly accepted as face-centred cubic at this temperature.¹² A. Taylor and D. Laidler¹³ have pointed out that graphite, when it is in a well-crystallised state, gives extra diffraction lines which have as yet received no convincing explanation. There is thus evidence that a survey of older work by the present more accurate methods would be well worth while.

Other improvements, such as the use of crystal-reflected radiation¹⁴ and of cameras of large resolution,¹⁵ have opened up a new and important field of investigation—the study of the intermediate structures that form during transformations in the solid state. Perhaps the most important investigations have been those of G. D. Preston¹⁶ and A. Guinier¹⁷ on the change with time of an alloy of 4% copper in aluminium. At 500° this alloy is a solid solution; at lower temperatures the copper is gradually precipitated. This precipitation is accompanied by changes in hardness, and the effect—known as “age-hardening”—has been widely discussed.¹⁸ From X-ray photographs, Preston and Guinier, independently but in striking agreement, have produced evidence of the exact nature of the precipitation, and this must form an important point in the ultimate explanation of the phenomenon.

The evidence is as follows. Photographs of a single crystal of the alloy quenched from 500° show faint streaks as well as the ordinary reflections. That these streaks are associated with structural changes in the alloy is shown by the fact that their intensity increases with time. The conclusion was reached that they are due to the formation of plates of copper atoms, and analysis showed that these plates must be parallel to the (100) planes of the aluminium lattice. The fact that the streaks are directed away from the origin confirms the suggestion that they are due to the precipitation of atoms smaller than aluminium, and from their lengths it was decided that the plates are only about two atoms thick.

Preston¹⁹ has continued the work by maintaining the crystal at 200° in the X-ray camera. As expected, the process continues at a faster rate than at room temperature; it also goes further, as the streaks, after becoming more intense, break up into spots. These, it was found, can be accounted for by the formation of a definite structure with a definite orientation with respect to the aluminium lattice. The atomic arrangement of this, however, is not the same as that of the θ phase²⁰ which has been established by D. Stockdale²¹ as the equilibrium structure. Instead, the atoms adopt the arrangement typified by calcium fluoride,²² and this is such that, with the orientation found, it fits neatly on the (100) planes of the aluminium lattice. The θ structure cannot do this, and so it appears that the presence

¹² S. Sekito, *Z. Krist.*, 1930, **74**, 189.

¹³ *Nature*, 1940, **146**, 130.

¹⁴ I. Fankuchen, *ibid.*, 1937, **139**, 193.

¹⁵ H. Lipson, *ibid.*, 1940, **146**, 798.

¹⁶ *Proc. Roy. Soc.*, 1938, *A*, **167**, 526.

¹⁷ *Compt. rend.*, 1938, **206**, 1641.

¹⁸ “Age Hardening of Metals,” 1940, Amer. Soc. for Metals, Cleveland.

¹⁹ *Phil. Mag.*, 1938, **26**, 855.

²⁰ J. B. Friauf, *J. Amer. Chem. Soc.*, 1927, **49**, 3107.

²¹ *J. Inst. Metals*, 1933, **52**, 111.

²² “Strukturbericht,” I, 1931, 148.

of ready-made structural elements in the parent lattice can favour the formation of a structure that is not the one of lowest free energy.

C. S. Barrett and A. H. Geisler²³ have made similar investigations of an alloy of 20% silver in aluminium. This alloy is also a single phase at 500° and its X-ray photographs also show streaks when it is quenched to room temperature. The orientations of these streaks show that the planes of precipitation are the {111} set, and this fits in well with the structure that is ultimately precipitated. This structure is that of Ag_3Al which has been shown by A. Westgren and A. J. Bradley²⁴ to be close-packed hexagonal with a random distribution of silver and aluminium atoms. It can therefore fit on to the cubic aluminium structure since both are formed of similar close-packed planes of atoms; the relative orientations agree with this suggestion. Barrett and Geisler think that there may be other explanations of the streaks, but G. D. Preston²⁵ has published more data which tend to confirm that given here.

C. Samans²⁶ has discussed the changes in the aluminium-copper alloy and has shown how the "calcium fluoride" structure can be derived from the plates of copper atoms formed initially.

The alloy Cu_3FeNi_3 has been shown by A. J. Bradley²⁷ to dissociate in a way which has some similarity to these other cases. In equilibrium at room temperature this alloy contains almost equal amounts of two face-centred cubic structures;²⁸ this state is formed by the splitting-up of a single face-centred cubic structure at about 800°. At temperatures below this, diffusion is not very rapid and the process of change is slow, so that by quenching the alloy after different times of annealing at about 700° it can be preserved in different stages of decomposition. X-Ray powder photographs of the alloy quenched from 800° show, of course, only one set of spectra, while those of the alloy annealed at 650° for one week show two sets due to the two phases. The intermediate structure, however, shows some lines (e.g., 222) that are double, as for the two-phase state, but others (e.g., 311) that have more components.²⁹ The explanation proposed by Bradley is that in this intermediate state two tetragonal structures exist with a common (001) face. These two structures are nearly cubic but one has an axial ratio greater than unity, the other, less. In this way the two structures preserve their respective atomic volumes and yet retain much of their relation to the parent cubic lattice.

A similar state of affairs has been found by electron diffraction for the deposition of aluminium on platinum.³⁰ The aluminium is constrained to adopt the slightly smaller spacing of platinum, but it preserves its atomic

²³ *J. Appl. Physics*, 1940, **11**, 733.

²⁴ *Phil. Mag.*, 1928, **6**, 280.

²⁵ *J. Sci. Instr.*, 1941, **18**, 154.

²⁶ *Amer. Inst. Min. Met. Eng.*, 1940, **137**, 85.

²⁷ *Proc. Physical Soc.*, 1940, **52**, 80.

²⁸ W. Köster and W. Dannöhl, *Z. Metallk.*, 1935, **27**, 220; A. J. Bradley, W. F. Cox, and H. J. Goldschmidt, *J. Inst. Metals*, 1941, **67**, 189.

²⁹ A. J. Bradley, W. L. Bragg, and C. Sykes, *J. Iron Steel Inst.*, 1940, **141**, 113.

³⁰ *Proc. Roy. Soc.*, 1933, **A**, **141**, 398.

volume by becoming tetragonal with an axial ratio greater than unity. This tetragonal aluminium can, however, exist only as unstable thin films.

Imperfections of another sort have been found in cobalt. This is one of the few elements whose structural history has never been satisfactorily established,³¹ and specimens that have been heat-treated in the solid state usually contain two phases, face-centred cubic and close-packed hexagonal. The hexagonal phase gives a remarkable mixture of sharp and "fuzzy" diffraction lines, and the following explanation of this has been given by O. S. Edwards, H. Lipson, and A. J. C. Wilson.³²

Close-packed structures can be considered as composed of layers of close-packed atoms, each layer fitting neatly on the one below. Consideration of the figure shows that there are two possible positions in which

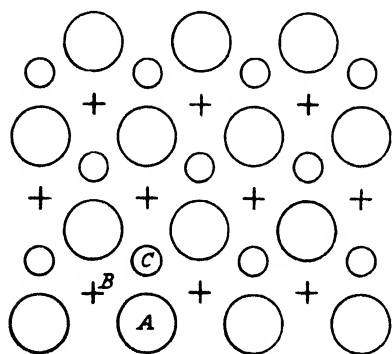


FIG. 1.

the second layer can fit on the first one, *A*; these two positions are shown as small circles and crosses respectively. Suppose the second layer goes into the *B* positions; then the third layer can take either the first position, *A*, or the position *C*. A close-packed structure can be built up of any random arrangement of types of planes *A*, *B*, and *C*, the only limitation being that no two successive planes shall be the same. In practice, however, only two arrangements are of importance: *ABCABCA* . . . which

is cubic, and *ABABABA* . . . which is hexagonal.

Hexagonal cobalt approximates to this second sequence, as is shown by the positions of lines on powder photographs. It is suggested,³² however, that mistakes occur occasionally, the sequence changing from *ABABABA* . . . to, say, *ACACACA* . . . Some of the reflections, such as the orders of 0001, will not be affected by the resultant faults; these remain sharp; but all others will be blurred to an extent depending on the average size of the regions of perfect sequence and on the orientation of the reflecting planes.

Oscillation photographs of cobalt³³ bring out the peculiarity of the structure very markedly. The sharp reflections are represented by ordinary spots; the others are drawn out into streaks which nearly merge into one another forming long lines on the photographs with periodic maxima and minima.

It is interesting that Barrett and Geisler²³ have suggested this same defect as a possible cause of the streaks on their silver-aluminium photographs.

³¹ A. E. van Arkel, "Reine Metalle," 1939, p. 327, Berlin.

³² *Nature*, 1941, **148**, 165.

³³ O. S. Edwards and H. Lipson, *Proc. Roy. Soc.*, 1942, *A*, (in press).

The general use of *X*-rays in the study of the properties of metals and alloys has been well summarised by several recent publications. On the determination of equilibrium diagrams there are papers by A. J. Bradley, W. L. Bragg, and C. Sykes,³⁴ and by W. Hume-Rothery,³⁵ both summarising several years' work by their respective schools. The report of a conference on "Internal Strains in Metals,"³⁶ organised by the Physical Society, contains many papers on *X*-ray investigations, particularly by W. A. Wood and by G. W. Brindley on distorted lattices; it also contains, in greater detail, much of the material in the present report. Finally, the Institute of Physics has collected together a number of papers on the application of *X*-rays to industrial problems,³⁷ and on particular branches of *X*-ray technique.³⁸ These papers taken together form a useful review of the present state of development in the use of *X*-rays for the examination of metals.

H. L.

4. INORGANIC STRUCTURES.

In a general discussion of the presentation of crystal chemistry, A. F. Wells¹ suggests that the most satisfactory classification of crystal structures for this purpose is one which is primarily geometrical, and based as far as possible on observed interatomic distances. In a classification of the kind described, the first division, following Weissenberg, is into four groups, in which the complexes that may be distinguished in the structure are finite, or infinite in one, two, or three dimensions. The recognition of the complex rests largely on interatomic distances, supported by the properties of the crystal. Sub-divisions are then made according as there are in the crystal, structural units all of one kind or of more than one kind; further sub-divisions arise according as the complexes are joined by van der Waals, hydrogen, or ionic bonds. The recognition of a particular type of geometrical complex does not imply any special bond type—inert gases, metals and alloys, and ionic and homopolar crystals are all classed under crystals containing 3-dimensional complexes—but the scheme is designed to allow a discussion of the nature of the bonds in a given structure without the issue having been prejudged.

Critical reviews of the classification of structures according to bond type and of the sub-division of ionic structures according to electrostatic bond strength are included, and the treatment of these topics in recent textbooks of crystal chemistry is discussed. In the detailed classification given, the chlorite minerals are by accident omitted as the example of a class containing infinite two-dimensional ions of opposite charge. In another paper² finite complexes in crystals are classified according to the number and

³⁴ *J. Iron Steel Inst.*, 1940, **141**, 63.

³⁵ Research Reports of the British Non-Ferrous Metals Research Association, 1941, No. 562.

³⁶ *Proc. Physical Soc.*, 1940, **52**, 1.

³⁷ *Ibid.*, p. 126.

³⁸ A. F. Wells, *ibid.*, 1940, [vii], **30**, 103.

³⁷ *J. Sci. Instr.*, 1941, **18**, 69.

¹ *Phil. Mag.*, 1941, [vii], **32**, 106.

arrangement of the atoms of one kind only, this being in general the more electropositive atom.

K. Fajans³ discusses the effect of polarisation of ions on the departure of interionic distances from additivity in the oxides, fluorides, and hydrides of the alkali metals and the oxides and fluorides of calcium, strontium, and barium. The difference between the metal-oxygen and the same metal-fluorine ion separations increases in the alkali-metal salts from lithium to potassium, i.e., in the order of increasing radius and decreasing field strength of the alkali ion; the same is true for the difference between metal-hydrogen and metal-fluorine distances, and a similar result is found in the comparison of the oxides and fluorides of the doubly charge cations Ca^{++} , Sr^{++} , and Ba^{++} . Since O^{--} and H^- are more polarisable than F^- , it is concluded that the decrease in size of anion in the field of the cation contributes distinctly to the deviations from additivity. Further, since the difference between the hydride and fluoride separations has a maximum for the rubidium compounds, there is a second effect which is interpreted as a stronger "loosening" action of F^- compared to H^- on the more easily polarisable of the cations.

V. Schomaker and D. P. Stevenson⁴ propose a revision upwards of the covalent single-bond radii of fluorine, oxygen, and nitrogen. They suggest $N = 0.74$ (0.70), $O = 0.74$ (0.66), $F = 0.72$ (0.64); the figures in parentheses are those of L. Pauling and M. L. Huggins.⁵ With the new values, which are based on electron-diffraction results for hydrazine,⁶ hydrogen peroxide,⁶ and fluorine,^{7, 8} many bond lengths which formerly obeyed the additivity rule are now less than the sum of the covalent radii $r_A + r_B$. The bond length r_{AB} is obtained from the expression

$$r_{AB} = r_A + r_B - \beta(x_A - x_B);$$

$\beta = 0.09$, x_A and x_B are the values of the Pauling electronegativities of the bonded atoms. It is inferred that the deviation from additivity represented by $-\beta(x_A - x_B)$ is associated with the extra ionic character of the bond A-B as compared to the ionic character of the normal covalent bond between like atoms.

W. Hume-Rothery and G. V. Raynor⁹ discuss the apparent sizes of atoms in metallic crystals with special reference to aluminium and indium, and the electronic state of magnesium.

Recent Structures.—From X-ray diffraction by liquid and plastic sulphur at temperatures from 124° to 340° N. S. Gingrich¹⁰ has obtained atomic distribution curves. The nearest neighbour for an atom in plastic sulphur is at 2.08, and at approximately 2.07 Å. for liquid sulphur at all temperatures. In plastic sulphur each atom has two near neighbours, and the

³ *J. Chem. Physics*, 1941, **9**, 281.

⁴ *J. Amer. Chem. Soc.*, 1941, **63**, 37.

⁵ *Z. Krist.*, 1934, **87**, 205.

⁶ P. A. Giguere and V. Schomaker, quoted in (4).

⁷ L. O. Brockway, *J. Amer. Chem. Soc.*, 1938, **60**, 1348.

⁸ M. T. Rogers, V. Schomaker, and D. P. Stevenson, *ibid.*, 1941, **63**, 2610.

⁹ *Proc. Roy. Soc.*, 1940, **A**, 177, 27.

¹⁰ *J. Chem. Physics*, 1940, **8**, 29.

estimated number of neighbours for liquid sulphur is 1.7. This shows that liquid sulphur is not a close-packed liquid, such as mercury. Also, if all the liquid consisted of closed rings, 2 near neighbours should be found and the observed 1.7 means that an average of 30% of the atoms have one neighbour only. The physical properties preclude the presence of S_2 molecules, but if the S_8 rings, that exist in the solid, break into chains on melting, this gives approximately the right proportion of atoms with only one near neighbour. The disrupted rings may join to form irregular chains with larger numbers of atoms.

A. H. White and L. H. Germer¹¹ have made electron-diffraction experiments on extremely small crystallites of carbon deposited on silica by pyrolysis of methane, and conclude that this carbon-black consists of pseudo-crystals, in each of which carbon atoms are hexagonally arranged, as in graphite, but successive atomic layers are displaced so that no regularities exist other than the uniform separation of the planes, and the regular arrangement of atoms in each of these. The spacing between planes is found to be 3.6 Å., 9% larger than the spacing, 3.35 Å., in graphite crystals.

The unit cell and space-group of jamesonite, $4PbS, FeS, 3Sb_2S_3$, have been determined, from single-crystal photographs.¹² Powder photographs agree with those previously published, and it is shown that a previous attempt¹³ to obtain the dimensions of the large monoclinic cell failed owing to the inherent limitations of the powder method. By electron-diffraction methods I. H. Usmani¹⁴ finds that copper sulphide film formed electrolytically and film formed by direct action of hydrogen sulphide on copper crystals give structures which do not agree with the structure of either cuprous or cupric sulphide as given by X-ray studies.

A re-examination of lead monoxide by W. J. Moore and L. Pauling¹⁵ has proved that the structure of the red tetragonal form is that previously reported by R. G. Dickinson and J. B. Friauf,¹⁶ and not that of G. R. Levi and E. G. Natta.¹⁷ In the structure now confirmed each oxygen has four lead atoms arranged tetrahedrally around it and each metal atom is bonded to four oxygens which form a square to one side of it. It is suggested that the orbital arrangement of Pb^{II} (and of Sn^{II}) is that of a square pyramid with four bonds directed from the metal within the pyramid towards the four corners of the base, and a fifth orbital occupied by a stereochemically active unshared pair, directed towards the apex. This stereochemical type is in contrast with the trigonal bipyramid arrangement found for many other compounds where the valency group is a decet, and it would be of great interest to know whether it persists in finite complexes, or whether, like the trigonal prismatic arrangement for six bonds, it is confined to giant molecules as in this structure. Stannous oxide has a similar structure to

¹¹ *J. Chem. Physics*, 1941, **9**, 492.

¹² J. E. Hiller, *Z. Krist.*, 1938, **100**, 128.

¹³ *J. Amer. Chem. Soc.*, 1941, **63**, 1392.

¹⁴ *Ibid.*, 1924, **46**, 2457.

¹⁵ L. G. Berry, *Min. Mag.*, 1940, **25**, 597.

¹⁶ *Phil. Mag.*, 1941, [vii], **32**, 89.

¹⁷ *Nuovo Cim.*, 1926, **3**, (3).

lead monoxide, but palladous and platinous oxides, though tetragonal, have a structure quite different in its essentials, which are that it is a compromise arrangement whereby each metal atom has four neighbours at the corners of a rectangle, $O-M-O = 82^\circ$ and 98° , and each oxygen has four nearly tetrahedral neighbouring metal atoms, $M-O-M = 98^\circ$ and 116° ; $Pd-O = 2.01 \pm 0.01$, $Pt-O = 2.02 \pm 0.02$.

Tellurite, TeO_2 ,¹⁸ has a structure resembling that of brookite (TiO_2), each tellurium being surrounded octahedrally by six oxygens. The relative disposition of octahedra is the same as in brookite but is greatly deformed. In lithium hydroxide monohydrate¹⁹ each lithium is at the centre of a tetrahedron of oxygens and two such tetrahedra share an edge in a reflection plane while the upper and lower corners are shared with tetrahedra in the unit cells above and below, resulting in unending chains of paired tetrahedra along one axis of the crystal. These chains are linked sideways by hydroxyl bonding. Between corners of adjacent tetrahedra the $O-O$ distance is 2.68, and there are therefore hydroxyl bonds here, two reaching from each oxygen to other oxygens. The oxygens of the shared tetrahedron edges in the reflection plane are shown to be in hydroxyl groups, and the oxygens of the upper and lower tetrahedron corners are in water groups. The tetrahedra are linked sideways by hydroxyl bonding between the hydroxyls and water. Observed interatomic distances are:

$Li-O_{OH}$ 1.95, $Li-O_{H_2O}$ 1.97, $O_{OH}-O_{H_2O}$ 2.68, $O_{OH}-O_{OH}$ 3.74, $O_{H_2O}-O_{H_2O}$ 3.48 Å.

The compound²⁰ $CoSe_2$ has metallic properties and the iron pyrites type of structure. The cube edge has $a = 5.845 \pm 0.005$. The interatomic distances now found are $Co-Se$ 2.43 ± 0.01 , $Se-Se$ 2.49 ± 0.04 . The latter value is a slight correction of an earlier reported value and is still 0.21 Å. greater than the $Se-Se$ distance in crystalline selenium.

The α -modification of iodic acid is orthorhombic. A structure determination by M. T. Rogers and L. Helmholz²¹ shows the existence of discrete IO_3 groups with $I-O = 1.80$ and 1.81 Å., and the $O-I-O$ angles 96° , 98° , and 101° . Three oxygen atoms in positions approximately opposed to the three bonded atoms are at distances 2.45, 2.7, and 2.95 Å. These complete a distorted octahedron of oxygen around the iodine, with three strong and three weaker bonds. In addition the HIO_3 molecules are held together by hydrogen bonds, the hydrogen atom of the hydroxyl group preferring in this structure to form two weak bonds (the bifurcated type)²² to two other oxygens, rather than one strong bond to one only of the available oxygen atoms.

Electron diffraction of nitric acid agrees with a planar model of the molecule.²³ There is an NO_2 group with $N-O = 1.22$ for both distances

¹⁸ T. Ito and H. Sawada, *Z. Krist.*, 1939, **102**, 13.

¹⁹ R. Pepinsky, *ibid.*, p. 119.

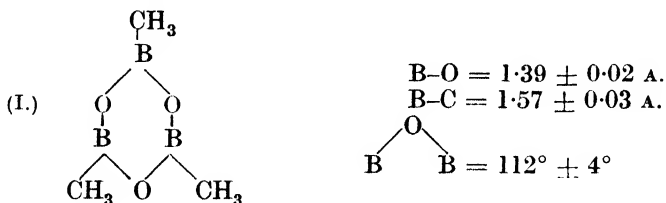
²⁰ B. Lewis and N. Elliott, *J. Amer. Chem. Soc.*, 1940, **62**, 3180.

²¹ *Ibid.*, 1941, **63**, 278.

²² See *Ann. Reports*, 1940, **37**, 193; 1939, **36**, 181.

²³ L. R. Maxwell and V. M. Mosley, *J. Chem. Physics*, 1940, **8**, 738.

and angle O-N-O = 130° , which is also found for nitrogen dioxide. The third oxygen is at 1.41 ± 0.02 A. from the nitrogen atom and equidistant from the other oxygen atoms. Methyl borate²⁴ has a planar BO_3 group with B-O = 1.38 ± 0.02 , O-C = 1.43 ± 0.03 A., and angle B-O-C = $113^\circ \pm 3^\circ$. Trimethyltriborane²⁴ has the structure (I), which is completely planar, except for the hydrogen atoms.



$\text{AlB}_3\text{H}_{12}$,²⁵ by electron diffraction, has aluminium bonded to BH_4 groups at angles of 120° , making the molecule planar except for the hydrogen. The boron atoms are located near the centres of trigonal bipyramids formed by the four hydrogen atoms of each BH_4 and the central aluminium: Al-B = 2.14 ± 0.02 , B-H = 1.24 ± 0.04 . Hexamethyldilead²⁶ gives by electron diffraction Pb-Pb = 2.88 ± 0.03 and Pb-C = 2.25 ± 0.06 and has a tetrahedral arrangement of the lead bonds. Electron-diffraction methods give values for interatomic distances in a large number of halides of elements of Groups II, IV, and VI. The cadmium halides²⁷ are probably linear, and Cd-Cl = 2.235 ± 0.03 , Cd-Br = 2.39 ± 0.03 , Cd-I = 2.56 ± 0.03 . The halides of bivalent tin and lead are not linear: Sn-Cl = 2.42 ± 0.02 , Sn-Br = 2.55 ± 0.02 , Sn-I = 2.73 ± 0.02 , Pb-Cl = 2.465 ± 0.02 , Pb-Br = 2.60 ± 0.03 , Pb-I = 2.79 ± 0.02 . In the tetrahalides²⁸ the distance from the central atom to halogen is for C-Br = 1.94 ± 0.02 , C-I = 2.15 ± 0.02 , Si-Br = 2.14 ± 0.02 , Si-I = 2.43 ± 0.02 , Ge-Br = 2.29 ± 0.02 , Ge-I = 2.50 ± 0.03 , Sn-Br = 2.44 ± 0.02 , Sn-I = 2.64 ± 0.04 , Ti-Cl = 2.18 ± 0.04 , Ti-Br = 2.31 ± 0.02 , Zr-Cl = 2.335 ± 0.05 , Th-Cl = 2.61 ± 0.03 .

There is some uncertainty regarding the value given for Se-Cl in the tetrachloride, which is not quoted here. The discussion given on the departures from additivity in these and other interatomic distances may require some modification in view of the proposed change in the standard covalent radii referred to above. For thionyl bromide, D. P. Stevenson and R. A. Cooley²⁹ find S-Br = 2.27 ± 0.02 , Br-O = 3.05 ± 0.03 , and Br-S-Br = $96^\circ \pm 2^\circ$.

Among structures containing complex ions is that of tetraphenylarsonium iodide,³⁰ where the arsenic bonds are strictly tetrahedral: As-C = 1.95 A.

²⁴ S. H. Bauer and J. Y. Beach, *J. Amer. Chem. Soc.*, 1941, **63**, 1394.

²⁵ *Idem, ibid.*, 1940, **62**, 3440.

²⁶ H. A. Skinner and L. E. Sutton, *Trans. Faraday Soc.*, 1940, **36**, 1209.

²⁷ M. W. Lister and L. E. Sutton, *ibid.*, 1941, **37**, 406.

²⁸ *Idem, ibid.*, p. 393.

²⁹ *J. Amer. Chem. Soc.*, 1940, **62**, 2477.

³⁰ R. C. L. Mooney, *ibid.*, p. 2955.

Details of the phosphorus pentachloride structure,³¹ which is roughly of the caesium chloride type with PCl_4^+ and PCl_6^- ions, are the distances $\text{P}-\text{Cl} (\text{PCl}_4) = 1.98$, $\text{P}-\text{Cl} (\text{PCl}_6) = 2.06$ Å. Barium fluosilicate and fluo-germanate³² have a 1-molecule rhombohedral cell in a structure with a formal resemblance to caesium chloride, containing Ba^{++} and a nearly regular octahedral complex anion. Bunsen's salt³³ has the constitution $(\text{NH}_4)_6\text{Fe}(\text{CN})_6\text{Cl}_2$, with a regular octahedral ferrocyanide ion and distinct Cl^- ions. The structure of hexamethylisonitriliferrous chloride,³⁵ $\text{Fe}(\text{CN}\cdot\text{CH}_3)_6\text{Cl}_2\cdot 3\text{H}_2\text{O}$, gives a clue to the constitution of the ferrocyanides.³⁴ The hexagonal structure gives an accurate view of the octahedral complex cation with the atoms linked in the order FeCNC : $\text{Fe}-\text{C} = 1.85$, $\text{C}-\text{N} = 1.18$ Å. The iron-carbon distance is approximately that calculated for a 50% single-double bond character of the link, as in L. Pauling's suggested formula³⁵ for the ferrocyanide ion; the pure single- and double-bond lengths would be 2.0 and 1.79 Å., respectively. A bend of 7° at the nitrogen atom brings the methyl groups out of line with an otherwise linear sequence FeCNC , and provides additional evidence for the partial double-bond character, since, although the form $\text{Fe}-\text{C}\equiv\text{N}-\text{C}$ is naturally linear, the form $\text{Fe}=\text{C}=\text{N}\diagdown_{\text{C}}$ would bend at the nitrogen atom.

Further work by J. L. Hoard and W. J. Martin³⁶ on complex niobates has led to interesting results. They find that several salts which are obtained from but slightly different aqueous solutions contain complex niobate ions of different stereochemical types. K_3HNbOF_7 is an aggregate of K^+ , HF_2^- , and octahedral $[\text{NbOF}_5]^-$ ions; $\text{K}_2\text{NbOF}_5\cdot\text{H}_2\text{O}$ also contains the octahedral complex. In K_2NbF_7 the $[\text{NbF}_7]^-$ ion has the arrangement of seven bonds derived from the trigonal prismatic type for six bonds by the addition of an extra fluorine over one of the prism faces.³⁷ In K_3NbOF_6 , however, the group $[\text{NbOF}_6]^\equiv$ has the alternative configuration for a 7-co-ordinated complex, derived from the octahedron by addition of the seventh atom over the centre of an octahedron face, a configuration which is found in K_3ZrF_7 .³⁸ It appears therefore that these two 7-co-ordinated types are about equally stable, and it would not be surprising if both the $[\text{NbF}_7]^-$ and $[\text{NbOF}_6]^\equiv$ (or $[\text{ZrF}_7]^\equiv$) groups should be found in compounds where they have the opposite configurations to those so far found for them.

Apart from the case of lead and tin monoxides referred to above, the stereochemical type for a group of ten valency electrons is usually derived from the trigonal bipyramid, and a particularly interesting case is that

³¹ D. Clark, H. M. Powell, and A. F. Wells, in publication.

³² J. L. Hoard and W. B. Vincent, *J. Amer. Chem. Soc.*, 1940, **62**, 3126.

³³ H. M. Powell and G. W. R. Bartindale; see H. Irving and G. W. Cherry, *J.*, 1941, 25.

³⁴ H. M. Powell and G. W. R. Bartindale, in publication.

³⁵ "Nature of the Chemical Bond," 1939, p. 235.

³⁶ *J. Amer. Chem. Soc.*, 1941, **63**, 11. ³⁷ See *Ann. Reports*, 1939, **36**, 170.

³⁸ G. C. Hampson and L. Pauling, *J. Amer. Chem. Soc.*, 1938, **60**, 2702.

where there are four attached groups. The arrangement found for $[\text{IO}_3\text{F}_2]^-$ and suggested for TeCl_4 ³⁹ has now been observed by J. D. McCullough and G. Hamburger⁴⁰ for diphenylselenium bromide. The molecule approximates very closely to a trigonal bipyramid with the two bromine atoms opposed to each other at the apices, and the phenyl groups in two of the three equatorial positions: $\text{Br-Se-Br} = 180^\circ \pm 3^\circ$, $\text{C-Se-C} = 110^\circ \pm 10^\circ$, $\text{Se-Br} = 2.52 \pm 0.01$, $\text{Se-C} = 1.91 \pm 0.03$ Å.

Accurate quantitative methods of structure determination have been applied by S. H. Chao, A. Hargreaves, and W. H. Taylor⁴¹ to a typical orthoclase, and confirm the essential accuracy of the feldspar structures previously determined by qualitative methods. Co-ordinates for all atoms in the cell are determined to an accuracy probably better than 0.1 Å. The cell contents, $4\text{KAlSi}_3\text{O}_8$, are treated as containing two groups of atoms "8Si_I" and "8Si_{II}," which really comprise 12Si and 4Al atoms. In the tetrahedral group of oxygen around Si_I the Si-O distances are within the limits 1.66—1.70, and for Si_{II} the limits are 1.57—1.60 Å. It is assumed therefore that while the Si_{II} contain silicon only, the 8Si_I with the slightly larger average size of tetrahedron contain 4Si and 4Al atoms, with a random distribution among the atomic sites. The potassium ion is surrounded by nine oxygens in a group of rather irregular shape.

S. H. Chao and W. H. Taylor⁴² by a detailed examination find that there are different types of lamellar structure of the soda-potash feldspars according as the proportion of soda feldspar is less or greater than *ca.* 30%. The low-soda type comprises monoclinic potash feldspar with triclinic soda feldspar lamellæ in mutual orientation characteristic of pericline twins, and the high-soda structure comprises monoclinic potash feldspar with triclinic soda feldspar lamellæ orientated in accordance with the albite twin law. The same authors⁴³ find for the plagioclase feldspars of known compositions ranging from nearly pure soda feldspar to nearly pure lime feldspar, that X-ray observations are consistent with the existence of two separate isomorphous series. One, with the albite structure, extends from pure soda feldspar to at least 22% lime feldspar, the other with the anorthite structure extends from pure lime feldspar to 20—30% soda feldspar. In addition, there is a group of intermediate plagioclases recognisable by a characteristic arrangement of subsidiary layer lines in *c*-axis photographs. Experimental work, but as yet no complete structure, has been reported for tricalcium aluminate $3\text{CaO} \cdot \text{Al}_2\text{O}_3$.⁴⁴ The cell is cubic, $a = 15.235$ Å. Libethenite, $\text{Cu}_2(\text{OH})\text{PO}_4$,⁴⁵ has deformed PO_4 tetrahedra, a deformed octahedral arrangement of four oxygens and two hydroxyls around some copper atoms, and a pseudotrigonal-bipyramidal grouping of four oxygens and one hydroxyl

³⁹ *Ann. Reports*, 1940, **37**, 181.

⁴⁰ *J. Amer. Chem. Soc.*, 1941, **63**, 803.

⁴¹ *Min. Mag.*, 1940, **25**, 498

⁴² *Proc. Roy. Soc.*, 1940, **A**, **174**, 57.

⁴³ *Ibid.*, 1940, **A**, **176**, 76.

⁴⁴ L. J. Brady and W. P. Davey, *J. Chem. Physics*, 1941, **9**, 663.

⁴⁵ H. Heritsch, *Z. Krist.*, 1939, **102**, 1.

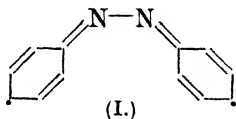
around other copper atoms, similar to the corresponding five-co-ordinated groups in andalusite, adamine, and olivenite.⁴⁶

From a study of absorption and fluorescent spectra of yttrifluorite, N. Chatterjee⁴⁷ concludes that solid solutions of yttrium fluoride in calcium fluoride are of the substitution type, since the interstitial type would produce greater disturbances than are observed in the spectra. The substitution lattice persists up to 50% of YF_3 , but above this other crystal types develop. This trifluoride itself is not cubic. A. L. Greenberg and G. H. Walden⁴⁸ studied the system $\text{KMnO}_4\text{--KClO}_4\text{--H}_2\text{O}$ by equilibrium and X-ray methods. In the continuous series of solid solutions of the salts, Vegard's additivity law is followed for the a and the c unit cell dimensions but not for b . The system $\text{NH}_4\text{Cl--MnCl}_2\text{--H}_2\text{O}$ shows three solid-solution series. In one of these, interstitial inclusion of manganese in the ammonium chloride lattice is accompanied by random substitution of water for NH_4^+ to maintain electrical neutrality. The compound $2\text{NH}_4\text{Cl, MnCl}_2, 2\text{H}_2\text{O}$ is similar in structure to the corresponding cupric compound. It has been found⁴⁹ that the alkali sulphates $\alpha\text{-K}_2\text{SO}_4$, $\alpha\text{-Na}_2\text{SO}_4$, and glaserite, $(\text{K, Na})_2\text{SO}_4$, constitute an isomorphous series of simple hexagonal structure with the alkali alkaline-earth phosphates $\text{M}'\text{M}''\text{PO}_4$, and with the calcium phosphate-silicates, $\text{Ca}_x(\text{SiO}_4)_y\text{PO}_4$, and the series may be expected to include other XO_4 groups.

H. M. P.

5. ORGANIC STRUCTURES.

Very few new structures have been fully determined by accurate methods since the last Report. A detailed analysis of the *cis*-form of azobenzene has now been completed¹ and the results of the Fourier analysis confirm in general the conclusions reported in the earlier analysis.² The main interest of this structure lies in the dimensional effects due to suppression of resonance. The molecule is unable to attain a planar configuration, and hence structures of the type (I) cannot make any large contribution



to the normal state. This is reflected in a measured C-N distance of 1.46 Å. (± 0.03) as compared with a corresponding distance of 1.41 Å. in the molecule of the *trans*-form.³ There is also apparently a small distortion in the normal valency angles (N-C-C) in a direction which permits the two benzene rings to become as nearly coplanar as possible, while the approach of the non-bonded carbon atoms is maintained at 3.3—3.4 Å.

⁴⁶ See *Ann. Reports*, 1937, **34**, 166.

⁴⁷ *Z. Krist.*, 1940, **102**, 245.

⁴⁸ *J. Chem. Physics*, 1940, **8**, 645.

⁴⁹ M. A. Bredig, *J. Amer. Chem. Soc.*, 1941, **63**, 2533.

¹ G. C. Hampson and J. M. Robertson, *J.*, 1941, 409.

² *Ann. Reports*, 1939, **36**, 183.

³ J. J. de Lange, J. M. Robertson, and (Miss) I. Woodward, *Proc. Roy. Soc.*, 1939, **A**, **171**, 398.

A very detailed study by electron-diffraction methods has been carried out on 1 : 3 : 5-tribromobenzene, 4 : 5-dibromo-*o*-xylene, 5 : 6-dibromohydrindene, and 6 : 7-dibromotetralin⁴ with a view to observe the effect of strain on the benzene ring (Mills-Nixon effect). In structures as complicated as these it is not possible in any sense to measure all the interatomic distances by electron diffraction, but the method consists rather in testing certain specified models. It is concluded that the Mills-Nixon effect is concerned primarily with changes in the contributions of the excited states of the molecule (which should lead to small but not easily measurable dimensional changes) and not with the "freezing" of the double bonds of the ring into a particular Kekulé structure.

An interesting quantitative study of a fibre diagram has been recorded for polyvinyl alcohol, $[-\text{CH}_2\cdot\text{CH}(\text{OH})-]_n$.⁵ About 30 reflections have been taken into account, and although the agreement between the measured and the calculated intensities is poor, yet the essential outlines of the structure appear to be clear. There are two chain segments ($\text{CH}_2\cdot\text{CH}\cdot\text{OH}$) in the unit cell (periodicity along the fibre axis, 2.52 Å.). The long chains of the molecule are so oriented that pairs of chains are linked through hydroxyl bonds.

Preliminary X-ray studies have been recorded for a number of compounds. Amongst these may be mentioned an extensive study of thianthren, selenanthren, phenazine, diphenylene dioxide, and related compounds by R. G. Wood and co-workers.^{6, 7, 8} The structural work on these compounds should be of interest in view of existing work on their dipole moments,^{9, 10} and the unsuccessful attempts which have been made to accomplish their optical resolution,¹¹ which have been attributed to insufficient rigidity in the molecule. The present work brings to light certain interesting relationships in the crystal structures of these compounds, which do not appear to be too complicated for detailed analysis. Some possible structures are described, but as X-ray intensity measurements are not even mentioned, it would be quite unprofitable for us to discuss these at present.

The structure of melamine, $\text{C}_3\text{N}_6\text{H}_6$, has been discussed by (Miss) I. E. Knaggs and (Mrs.) K. Lonsdale,¹² the results being based on X-ray and magnetic measurements. The amide structure is based on the cyanuric ring, and is of a layer type similar to that of other compounds in this class. Amino-groups appear to be connected to the ring nitrogens of adjoining

⁴ A. Kossiakoff and H. D. Springall, *J. Amer. Chem. Soc.*, 1941, **63**, 2223.

⁵ (Miss) R. C. L. Mooney, *ibid.*, p. 2828.

⁶ R. G. Wood and J. E. Crackstone, *Phil. Mag.*, 1941, **31**, 62.

⁷ R. G. Wood, C. H. McCale, and G. Williams, *ibid.*, p. 71.

⁸ R. G. Wood and G. Williams, *ibid.*, p. 115.

⁹ G. M. Bennett and S. Glasstone, *J.*, 1934, 128.

¹⁰ (Miss) I. G. M. Campbell, (Mrs.) C. G. LeFèvre, R. J. W. LeFèvre, and E. E. Turner, *J.*, 1938, 404.

¹¹ G. M. Bennett, (Miss) M. Lesslie, and E. E. Turner, *J.*, 1937, 444.

¹² *Proc. Roy. Soc.*, 1940, A, **177**, 140.

molecules by means of weak hydrogen bridges. The results of more detailed X-ray measurements will be of interest.

Sorbic acid¹³ has been analysed to a first approximation by means of absolute intensity measurements, and the orientation of the molecules is confirmed by magnetic measurements, and by the shape and size of the diffuse spots occurring on well-exposed Laue photographs (see Section 2 of this Report). The magnetic anisotropy due to resonance in the conjugated carbon chain is shown to be about half as large as that in the benzene ring. The molecules, which are linked in pairs by hydrogen bonds, appear to lie in rather favourable positions for accurate interatomic-distance measurements, but detailed work in this direction has not yet been completed.

Symmetry determinations on a number of substituted stilbene and dibenzyl compounds¹⁴ have been carried out, with results of importance in structural chemistry. A preliminary account of the X-ray analysis of calycanine, $C_{16}H_{10}N_2$, and of a series of substituted diphenyls,¹⁵ and a full account of the structure of *dl*-alanine¹⁶ by accurate methods have been published, but details are not yet available.

Sterols.—It is only possible to refer very briefly to a comprehensive account of the crystallography and chemistry of some eighty sterol derivatives which has now been published by J. D. Bernal, (Miss) D. Crowfoot, and I. Fankuchen.¹⁷ Following Bernal's original X-ray studies,¹⁸ which gave a clue to the structural formula of cholesterol, the present work has been carried on parallel with much of the chemical work of the last eight years. The derivatives described belong mainly to the cholesterol and the ergosterol series, but include calciferol and other photo-derivatives of ergosterol, and some higher plant and animal sterols. Crystallographic and optical data for all these compounds are classified in a number of convenient tables, and a detailed study is made of the effect of substituents on the crystal structures. More detailed analyses, involving intensity observations and Patterson projections on the (010) planes, have been made for cholesterol chloride, bromide, and cholesteryl chloride hydrochloride, with results which confirm the earlier deductions regarding the shape and size of the sterol molecules, and give some indication of the arrangement of the carbon and halogen atoms in the ring system. No exact structural analysis determining the position of every atom in the molecule has yet been attempted. The present paper, however, is an essential preliminary to such an undertaking, because it indicates those compounds which are crystallographically simple enough to make such an attempt feasible. From this point of view alone the survey is of extreme value, because many of the

¹³ (Mrs.) K. Lonsdale, J. M. Robertson, and (Miss) I. Woodward, *Proc. Roy. Soc.*, 1941, A, 178, 43.

¹⁴ C. H. Carlisle and (Miss) D. Crowfoot, *J.*, 1941, 6.

¹⁵ A. Hargreaves and W. H. Taylor, *J. Sci. Instr.*, 1941, 18, 138.

¹⁶ H. A. Levy and R. B. Corey, *J. Amer. Chem. Soc.*, 1941, 63, 2095.

¹⁷ *Phil. Trans.*, 1940, A, 239, 135.

¹⁸ *Nature*, 1932, 129, 277.

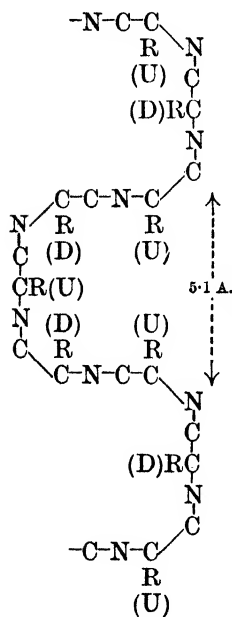
outstanding structural problems of the sterols can only be solved by such exact analyses.

Protein Structures: Keratin and Myosin.—Perhaps the most hopeful approach to any detailed picture of protein structure by X-ray methods lies in the study of the fibrous proteins keratin and myosin. Recently, Astbury and his co-workers^{19, 20, 21} have given a new impetus and orientation to this field by their revised discussion of the nature of the intramolecular fold in α -keratin and α -myosin. The earlier theory of the transformation which takes place when these fibres are stretched, involving the opening of hexagonal rings (incidentally, this led to D. Wrinch's cyclol hypothesis) has been abandoned in favour of a reversible intramolecular fold of the general type (II).

This kind of fold permits the close packing of the side chains (R) in a simple, regular pattern, alternately on one side and the other of the plane of the fold. The model may, in fact, be reached by deduction from the principle of close packing, which is necessarily involved on account of the very uniform densities of proteins in general. The various experimental and structural conditions, such as the long-range elastic properties, and the fold repeat distance of 5.1 Å., then become consequences of the close packing of the side chains. By means of such a model it is possible to account for the great range of chemical constitutions in the keratin-myosin group, merely by interchanging side-chain residues; moreover, the fundamental structural similarities, as revealed by X-rays, are explained by the invariable polypeptide skeleton.

More detailed analysis of the structure is now of great importance, and the data appear to be available in certain new and very perfect photographs by MacArthur²² on porcupine quill. In these photographs the striking feature that a large fibre axis periodicity and its dominant orders are found expressible in $2^m 3^n$ terms of the probable amino-acid length promises to be of great significance in elucidating the actual sequence of amino-acid residues.

(II.) *Plant-virus Preparations.*—J. D. Bernal and I. Fankuchen²³ have now published a very full preliminary account of their X-ray crystallographic work on tobacco-mosaic virus, enation-mosaic virus, aucuba-mosaic virus, cucumber



U = Side chain up.
D = Side chain down.

(II.)

¹⁹ W. T. Astbury and (Miss) F. O. Bell, *Nature*, 1941, **147**, 696.

²⁰ W. T. Astbury, *Chem. and Ind.*, 1941, 40, 41, 491.

²¹ W. T. Astbury, *J.*, 1942 (in publication) (Lecture to the Chemical Society, Nov. 20th, 1941).

²² *Wool Rev.*, 1940, 9; unpublished work.

²³ *J. Gen. Physiol.*, 1941, **25**, 111.

virus, potato virus, and tomato bushy-stunt virus. The tobacco-mosaic virus preparations were studied in most detail, and the recorded data refer chiefly to them. These preparations have a remarkable capacity for forming doubly refracting aggregates. In dilute solution they exhibit flow orientation and other peculiarities indicating the presence of long, thin particles. In concentrated solution the orientation is spontaneous, and in fact any small region behaves like a uniaxial positive crystal. X-Ray investigation shows that even in solution the particles are equidistant, the distance between them depending on the concentration. At concentrations of 30% and over, gel-like properties are found, and the preparations become stiffer as the water content decreases, but there are no abrupt transitions. The forces maintaining the particles equidistant and parallel in the gel are attributed to the ionic atmospheres surrounding them, and there is no doubt that the results obtained in this field will have wide extensions to other colloid systems.

In the dry gel the interparticle distance is 152 Å. The arrangement is so perfect that each specimen is in fact a two-dimensional single crystal. It is concluded from the evidence that the virus preparations consist of particles of about 150 Å. in diameter and with a minimum length of 1500 Å.²⁴ These extraordinary particles are in a sense intermediate between the molecule and the crystal. With regard to inner structure there is evidence of the existence of sub-units of approximately 11 Å.³ fitted together in a hexagonal or pseudo-hexagonal lattice of dimensions $a = 87$ Å., $c = 68$ Å. The particle itself seems to be virtually unchanged by drying, and so must contain but little water. In the case of bushy-stunt tomato virus there is evidence of spherical rather than long particles, and so it seems likely that the elongated particle form has no essential biological significance.

J. M. R.

H. LIPSON.

(Mrs.) K. LONSDALE.

H. M. POWELL.

J. M. ROBERTSON.

²⁴ G. A. Kausche, E. Pfankuck, and H. Ruska, *Naturwiss.*, 1939, **27**, 292.

ORGANIC CHEMISTRY.

I. INTRODUCTION.

A DISCUSSION on the "Mechanisms and Chemical Kinetics of Organic Reactions in Liquid Systems" was held by the Faraday Society in September, 1941, and the complete text of the various contributions is now available.¹ A wide field was covered, including aliphatic substitution, elimination reactions, esterification and hydrolysis, additions to olefinic compounds, nuclear and side-chain substitution in aromatic compounds, condensations of carbonyl compounds, prototropic and anionotropic changes, the Cannizzaro and the Friedel-Crafts reaction, ring closure, and reactions involving radicals. Many of these have been dealt with in the *Annual Reports* of 1938—40, and in Part 2 of the present section some recent investigations of condensations, alkylation reactions, rearrangements, and the influences of groups in *ortho*-positions are summarised. The values of dissociation constants in a single solvent and at an arbitrarily fixed temperature have long been accepted as providing a correct series of relative strengths of acids and bases, and hence of the polar effects of substituents; the justification for this conventional view is examined in this Report.

Systematic organometallic chemistry has been extended by the discovery, in triethylscandium and triethylttrium, of the first purely organic derivatives of the transitional elements (*i.e.*, those "framed" in Bohr's Periodic Table) showing the group valency. Gallium and indium compounds have been studied in more detail, the simple organic types R_3Tl and Me_4Pt have been prepared, and organic derivatives of titanium, vanadium, tantalum, molybdenum, tungsten, manganese and rhenium are reported. The formulation of the curious phenylchromium compounds has been reconsidered, and that of the dimeric trimethylaluminium presents a problem in valency theory. Numerous compounds of the heavy metals have been prepared from $R \cdot B(OH)_2$, $R \cdot SO_2H$, $R \cdot HgCl$ or especially $R \cdot N_2Cl$, by treatment with the metallic halide; in this way it is possible to prepare organometallic compounds containing hydroxyl or other reactive substituents. Alkyl, and sometimes aryl, residues attached to mercury or elements of the tin group undergo remarkably facile disproportionation in presence of catalysts; *e.g.*, $Me_2Hg + Et_2Hg \rightleftharpoons 2MeEtHg$. All this work is dealt with in Part 3 of this section.

It is now possible to present a general picture of the chief structural patterns upon which the natural polysaccharides are built, and to pick out certain definite types (see Part 4). The polysaccharides may be described as "simple" or "complex" according to whether they are composed of the same or varied monosaccharide building units; thus, starch could be

¹ *Trans. Faraday Soc.*, 1941, **37**, 601.

described as "simple" in that it is composed solely of glucose, whereas arabic acid is "complex," being constituted of galactose, glucuronic acid, arabinose, and rhamnose. A second method of classification depends upon the observation that in many well-known polysaccharides the glycosidic linkages between monosaccharide units are mainly or entirely of one type. For example, only β -1 : 4-glycosidic links occur in cellulose, α -1 : 4-links in pectic acid, and β -1 : 4-linkages in alginic acid. On the other hand, the arabans which are found in constant association with pectins are composed of arabofuranose residues combined by 1 : 5- as well as by 1 : 3-glycosidic links; yeast mannan is constituted solely of mannopyranose units, but three types of linkage, 1 : 2, 1 : 3, and 1 : 6, are present; in arabic acid, 1 : 3-, 1 : 6-, and 1 : 4-links are found. Damson gum, which is probably built on the same structural pattern as arabic acid, is known to contain 1 : 2-glycosidic linkages; this type of union is commonly associated with mannose residues, just as 1 : 3-links are often found associated with galactose (*e.g.*, in agar) and 1 : 4-links with glucose. A third basis for the classification of polysaccharides is illustrated as follows. Cellulose, starch, pectic acid, alginic acid, laminarin, and dextrans have unbranched chains of monosaccharide residues, but in many other polysaccharides the repeating units are more or less highly ramified structures, a feature which is shown particularly by the plant gums (*e.g.*, gum arabic, damson or cherry gum), and found also in the simple arabans, galactans, yeast mannan, in the polysaccharide associated with β -amylase, and in the mucilages. Snail galactogen (containing *d*- and *l*-galactose) differs from agar in possessing a branched-chain repeating unit. The plant gums and the mucilages are therefore "complex" in two senses; they contain more than one type of monosaccharide unit and these are united by more than one kind of glycosidic linkage. In addition, these natural products are acid polysaccharides, the acid character being contributed by the uronic acid residues, glucuronic acid in the former and galacturonic acid in the latter. In all the substances mentioned above, the repeating units contain one residue with a free reducing group and it is by virtue of this that aggregation takes place. A carbohydrate isolated from egg-albumin is of great interest in that, although it is constituted on a similar plan to the others, it appears not to be a true polysaccharide; the smallest unit in its structure is composed of eleven monosaccharide residues and does not display a free reducing group. This compound is perhaps more correctly described as a non-reducing hendecasaccharide; about 60% of it is composed of *N*-acetylglucosamine, the remaining residues being of mannose and galactose.

The most recent development in the chemistry of starch has been the recognition of the probability that it contains at least two components which are structurally different. One of these, amylopectin (or erythro-amylose), forms 80—95% of the whole starch, and is composed of aggregations of repeating units which are themselves constituted of chains of 24—30 glucose residues linked by α -1 : 4-glycosidic bonds. It has now been demonstrated that the polymeric links between the repeating units are α -1 : 6-

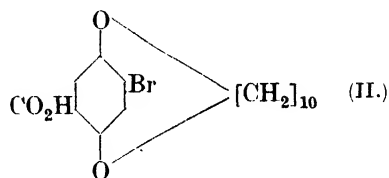
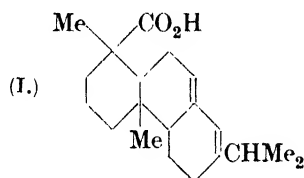
glycosidic. The second component of starch (amylose or amyloamylose) appears to be composed of much longer chains (100—300 glucose members), which may not form aggregates; it is perhaps identical with Hanes's synthetic starch, the chain-length of which has been shown to be at least 80 to 90 glucose residues. Amylose and synthetic starch are each degraded completely to maltose by β -amylase, whereas with amylopectin the degradation ceases at 60% conversion.

Part 5 of this section reviews recent studies of the synthesis of aliphatic and aromatic compounds containing a multiplicity of conjugated ethylenic linkages (polyenes), which have led to the discovery of new synthetic routes and also to the improvement and extension of the classical synthetic methods. Investigations have also been directed towards the synthesis of the more complicated naturally occurring polyenes such as the carotenoids and vitamin A, and although no outstanding successes have as yet resulted, the preparation of material possessing some vitamin A activity has been reported and a number of promising intermediates have been obtained. Aldehyde condensations of fundamental importance in the synthetic polyene field, particularly those of citral with aldehydes, have been investigated in some detail from the preparative aspect. Higher polyene carboxylic acids have been made available, and from them direct syntheses of palmitic and stearic acids have been achieved. Two new routes to the polyene dicarboxylic acids have also been developed, a biological preparation presenting novel features.

A considerable number of papers on polyterpenes have appeared during the period under review; these are distributed fairly evenly between sesquiterpenes and allied substances, diterpenes and triterpenes. In view of limitations of space, Part 6 of this section deals only with abietic acid and the β -amyrin and lupeol groups of triterpenes. The vexed question of the location of the ethylenic linkages in abietic acid has been finally settled by the elegant degradation experiments of Ruzicka and co-workers; the acid has the structure (I). Considerable progress has been made in the β -amyrin group of triterpenes, although it cannot be claimed that the basic structure of the group has been elucidated. It now comprises at least ten members, each of which has been transformed into β -amyrin or an established derivative. Betulin has been converted into lupeol, and the long suspected difference between these triterpenes and the members of the β -amyrin group has been established by the proof that the former contain an isopropenyl side chain. The presence of this unsaturated centre means, according to Ruzicka and Rosenkranz, that the lupeol group cannot be hydrocarbon derivatives, a conclusion which invokes the isoprene rule.

Following the discussion of natural naphthaquinone pigments in the *Annual Reports* for 1939, a review is now given (Part 7) of the present state of knowledge of the large group of natural colouring matters which are derivatives of benzoquinone, naphthaquinone, phenanthraquinone, and anthraquinone. In the benzoquinone group, particular interest attaches

to the simple quinones produced by certain fungi and to perezone, which is closely related to the sesquiterpenes. Similarly, tanshinone I is noteworthy among the derivatives of phenanthrene, since the available evidence suggests a relationship with the diterpenoids. Degradative evidence has been adduced in favour of the view that the antihæmorrhagic vitamin K_2 is 3-difarnesyl-2-methyl-1:4-naphthaquinone, and work on the naphthaquinone pigments of sea urchin eggs has recently been extended. Echinochrome A, the sole pigment isolated from fully mature ovaries of *Arbacia*, is accompanied in ovaries collected at different seasons by echinochromes B and C; echinochrome A appears to exist in the eggs as a complex of high molecular weight, which is more potent than the free pigment in conferring motility on spermatozoa. Considerable attention has been devoted in recent years to the production of anthraquinone derivatives by moulds, and an account is given of pigments of this type isolated from *Helminthosporium*, *Penicillium*, and *Aspergillus* species. Investigations on mould pigments from *Penicillium* and on hypericin, the photodynamic pigment of St. John's wort, have revealed striking resemblances between them, and the interesting suggestion has been made that hypericin and oxypenicilliosin may be helianthrone derivatives.



The reactivity of heterocyclic nuclei towards cationoid and anionoid reagents, and of methyl side-chains towards aldehydes, has been discussed in general terms, and much experimental work reported. Numerous nuclear transformations of furans, pyrroles and the azoles are recorded, most of which depend upon ring fission and re-synthesis to another heterocyclic type. An interesting new case of stereoisomerism depends upon the hindered rotation of the substituted benzene nucleus of a quinol polymethylene ether (II) relatively to the (moderately) large ring. The simple oxygen-ring compound dioxadiene has been prepared. Interest in compounds related to vitamin E has led to a thorough study of methods for the synthesis of chromans and coumarans. Some twenty quinoline homologues have been isolated from straight-run gasoline; their structures have been established and show some curious regularities. Evidence is submitted that a nucleus C_6N_7 , consisting of three fused cyanuric rings, is present in melem, cyameluric acid and other long-known products of the pyrolysis of thiocyanates. The pterins, pigments occurring in the wings of butterflies and in other insects, are now found to be relatively simple compounds closely related to the purines; leuco- and xantho-pterins have been synthesised from 2:4:5-triamino-6-hydroxypyrimidine with oxalic and dichloroacetic acids respectively. These advances in the chemistry

of heterocyclic compounds are summarised in the final part (8) of this section of the report.

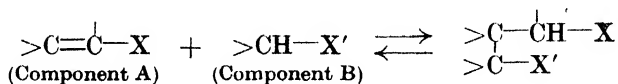
J. F. J. DIPPY.
E. R. H. JONES.
S. PEAT.
F. S. SPRING.
T. S. STEVENS.
A. R. TODD.
H. B. WATSON.

2. PHYSICO-ORGANIC TOPICS.

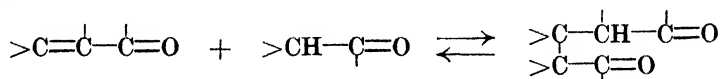
(a) *Mechanisms of Condensations and Alkylation Reactions.*

The mechanisms of condensations of the aldol, Knoevenagel, Perkin and Claisen types were discussed in the *Annual Reports* for 1939,¹ where reference was made to the recent work of C. R. Hauser and his collaborators.² W. G. Brown and K. Eberly³ have now investigated the base-catalysed exchange of hydrogen for deuterium between a number of esters and deuterioalcohol, EtOD, and they find that the facility of exchange may be correlated with the reactivity of the ester in the Claisen condensation. For a series of esters $R \cdot CH_2 \cdot CO_2Et$ where R is varied, the order is $Ph > H > Me > Et > Pr^a > C_{10}H_{21} > C_{16}H_{33} > cyclo-C_6H_{11} > Pr^b$; a second alkyl group as in $CHMe_2 \cdot CO_2Et$ leads to a further decrease in reactivity. The correlation is not a quantitative one, however, and the authors suggest that the influence of structure upon reactivity in the Claisen condensation is threefold, being manifested in the extent of the initial anion formation, the rate at which the anion reacts with the second ester molecule, and the extent to which the equilibrium is shifted by salt formation on the part of the β -keto-ester. A similar correlation between deuterium exchange and alkylation in malonic esters $R \cdot CH(CO_2Et)_2$ is suggested.

The investigations of C. R. Hauser and co-workers have been extended to include a study of reactions of the Michael type, *i.e.*, the addition of a compound having incipiently-ionised hydrogen at an olefinic linkage which is rendered susceptible to the attack of a nucleophilic reagent by an adjacent group :



In the most familiar examples, where X and X' are carbonyl or ester groupings, this becomes :



C. R. Hauser and B. Abramovitch⁴ represent this condensation (the revers-

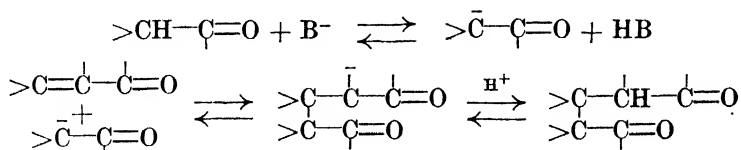
¹ *Ann. Reports*, 1939, **36**, 210.

² See also *J. Amer. Chem. Soc.*, 1940, **62**, 62, 593.

³ *Ibid.*, p. 113.

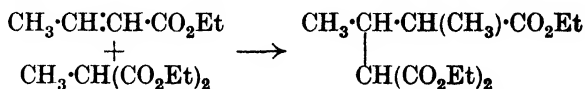
⁴ *Ibid.*, p. 1763.

ibility of which was demonstrated twenty years ago⁵) by a scheme which is completely analogous to that usually accepted for the aldol, Knoevenagel and Perkin reactions ($B^- = \text{OEt}'$, CPh_3' , or other basic catalyst):

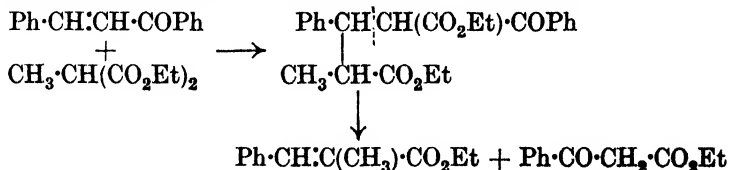


The factors which influence the Michael condensation, and the effects of structure upon reactivity, have been summarised by R. Connor and W. R. McClellan.⁶ The groups which may function as X or X' are CO_2R , COR , CHO , CN , $\text{CO}\cdot\text{NH}_2$, NO_2 , SO_2R (references to typical examples are quoted), and component A may be acetylenic rather than olefinic. The occurrence of other reactions (see below) is avoided by using as catalyst a secondary amine such as piperidine, but the change is slow, and long refluxing is necessary even in favourable cases; one-third to one-sixth of an equivalent of sodium ethoxide may bring about condensation where amines are ineffective (Hauser and Abramovitch used the still more powerful agent sodium triphenylmethyl), and long standing at room temperature now yields the best results. As solvent, methyl and ethyl alcohols, benzene, ether and dioxan have been used satisfactorily. Substituents in either component usually decrease reactivity,⁷ but there are exceptions and, as suggested originally by C. K. Ingold, E. A. Perren, and J. F. Thorpe,⁸ both spatial and polar influences may be involved.

Actually the products obtained under the conditions which lead to the Michael condensation are of three types: ⁹ (a) in presence of a small quantity of sodium ethoxide or piperidine the product is normal; (b) one equivalent of ethoxide leads, in some instances, to a "rearrangement product," *e.g.*,



(c) there are sometimes "rearrangement-retrogression products," which could arise from the cleavage of a rearrangement product, *e.g.*,



The formation of "rearrangement products," according to the views of J. F. Thorpe¹⁰ and of A. Michael and J. Ross,¹¹ depends upon the cleavage

⁵ C. K. Ingold and W. J. Powell, *J.*, 1921, **119**, 1976.

⁶ *J. Org. Chem.*, 1939, **3**, 570.

⁷ See also ref. 9.

⁸ *J.*, 1922, **121**, 1771.

⁹ See R. Connor and D. B. Andrews, *J. Amer. Chem. Soc.*, 1934, **56**, 2713.

¹⁰ *J.*, 1900, **77**, 923.

¹¹ *J. Amer. Chem. Soc.*, 1930, **52**, 4598.

of the substituted malonic ester into portions such as CH_3 and $\text{CH}(\text{CO}_2\text{Et})_2$, but N. E. Holden and A. Lapworth¹² postulate a normal addition, followed by migration of carbethoxyl (or similar group), a view which has been supported more recently by J. A. Gardner and H. N. Rydon.¹³

Although the most familiar condensations of the aldol, Knoevenagel, Perkin, Claisen and Michael types occur under the catalytic influence of bases (electron-donators), examples of catalysis by acids (electron-acceptors) are known. D. S. Breslow and C. R. Hauser¹⁴ have now carried out a number of condensations in presence of the electron-accepting agents boron fluoride and aluminium chloride. These include the condensation of acetic anhydride with acetophenone (Claisen type) and the condensation of benzaldehyde with malonic ester and with acetic anhydride (only a small yield of cinnamic acid was isolated, however). The reaction of benzaldehyde with ethyl malonate was followed by a Michael addition, giving ethyl benzylidene-dimalonate. In presence of boron fluoride, ethyl acetoacetate is alkylated both by benzyl chloride¹⁴ and by isopropyl acetate¹⁵ [giving

$\text{CH}_3\cdot\text{CO}\cdot\text{CH}(\text{CH}_2\text{Ph})\cdot\text{CO}_2\text{Et}$
and $\text{CH}_3\cdot\text{CO}\cdot\text{CH}(\text{CHMe}_2)\cdot\text{CO}_2\text{Et}$ respectively].

In a general discussion of reactions of the types referred to above, C. R. Hauser and D. S. Breslow¹⁶ point out that component B is always a compound having incipiently-ionised hydrogen, and component A may be an alkyl halide (alkylation of ethyl acetoacetate, etc.), an aldehyde or ketone (aldol, Knoevenagel, Perkin), an ester, anhydride or acid chloride (Claisen), or a suitably activated olefinic compound (Michael). In accordance with the usually accepted view,¹ they suppose that bases activate component B by converting it into anion, whereas acidic (electron-accepting) catalysts activate component A by forming a co-ordination complex. For a given component A, the ease of condensation should follow the activity of the labile hydrogen of component B, and they quote examples to show that such is the case. Further, compounds which are not sufficiently reactive to function as component A in presence of a base might do so under the influence of an acid catalyst, and it is found that both diisopropyl ether and isopropyl alcohol condense with acetoacetic ester in presence of boron fluoride. Hauser and Breslow envisage the possibility of an attack of the catalyst upon *both* reacting substances; for example, an acidic catalyst might, in addition to activating component A, also co-ordinate with carbonyl oxygen in component B, and a basic catalyst might form an addition complex with component A. The last possibility was considered in the *Annual Reports* for 1939.¹ If the base co-ordinated with component A to give a complex possessing sufficient energy to react with component B, the energy of activation would be needed for the formation of this complex, and would be influenced by constitutional changes in A, but almost indifferent to changes in B. This is actually the case in the reaction of benzaldehyde

¹² *J.*, 1931, 2368.

¹³ *J.*, 1938, 48.

¹⁴ *J. Amer. Chem. Soc.*, 1940, **62**, 2385. Compare H. Meerwein, *Ber.*, 1933, **66**, 411.

¹⁵ *J. Amer. Chem. Soc.*, 1940, **62**, 2611. ¹⁶ *Ibid.*, p. 2389.

with acetophenone in 90% alcohol with sodium ethoxide as catalyst.¹⁷ There are, however, objections to this mechanism of basic catalysis,¹⁸ and further experimental studies are necessary.

The rate of the reaction of benzaldehyde with acetophenone is proportional to the concentrations of both;¹⁷ on the other hand, the aldol condensation of acetaldehyde is of the first order with respect to the aldehyde, and the corresponding reactions of acetone and *isobutyraldehyde* are of the second and an intermediate order respectively.¹⁹

The influence of aluminium chloride and boron fluoride upon these condensations, referred to on p. 117, finds an analogy in the catalytic effect of boron fluoride in the esterification of acetic, propionic and a number of aromatic acids by various alcohols, observed by J. A. Nieuwland and co-workers,²⁰ who suggest that the mechanism is doubtless similar to that of the hydron-catalysed reaction; addition compounds of boron fluoride with acids, alcohols, and esters are known to exist.²¹ Esters are also formed when alcohols react with amides in presence of boron fluoride,²² and by the reaction of acids with olefins under the influence of the same catalyst;²³ boron fluoride also catalyses the acidolysis of esters.²⁴

A consideration of some aspects of the Friedel-Crafts reaction forms a natural sequel to the above, although boron fluoride is apparently not effective in nuclear alkylation by alkyl halides,²⁵ nor has it been employed in acylations by the Friedel-Crafts method. In the *Annual Reports* for 1937,²⁶ reference was made to the use of substances other than alkyl halides (alcohols, ethers, esters, olefins) for alkylation in presence of aluminium chloride, and similar processes have been carried out with boron fluoride as the catalyst. For instance, benzene,²⁷ phenol,²⁸ anisole²⁹ and all three hydroxybenzoic acids³⁰ have been converted into nuclear *isopropyl* derivatives by propylene in presence of boron fluoride (in the case of phenol and the hydroxybenzoic acids, etherification or esterification may be followed

¹⁷ (Miss) E. Coombs and D. P. Evans, *J.*, 1940, 1295.

¹⁸ See discussion on the Mechanism and Chemical Kinetics of Organic Reactions in Liquid Systems, *Trans. Faraday Soc.*, 1941, **37**, 718.

¹⁹ R. P. Bell, *ibid.*, p. 716.

²⁰ H. D. Hinton and J. A. Nieuwland, *J. Amer. Chem. Soc.*, 1932, **54**, 2017; F. J. Sowa and J. A. Nieuwland, *ibid.*, 1936, **58**, 271.

²¹ H. Bowlus and J. A. Nieuwland, *ibid.*, 1931, **53**, 3835.

²² F. J. Sowa and J. A. Nieuwland, *ibid.*, 1933, **55**, 5052.

²³ T. B. Dorris, F. J. Sowa, and J. A. Nieuwland, *ibid.*, 1934, **56**, 2689; T. B. Dorris and F. J. Sowa, *ibid.*, 1938, **60**, 358.

²⁴ F. J. Sowa, *ibid.*, p. 654.

²⁵ A. Wohl and E. Wertyporoch, *Ber.*, 1931, **64**, 1357.

²⁶ P. 260. Compare N. O. Calloway, *Chem. Reviews*, 1935, **17**, 327; (Miss) D. V. Nightingale, *ibid.*, 1939, **25**, 329.

²⁷ S. J. Slanina, F. J. Sowa, and J. A. Nieuwland, *J. Amer. Chem. Soc.*, 1935, **57**, 1547.

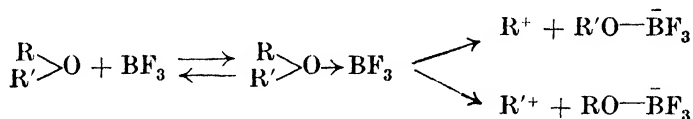
²⁸ F. J. Sowa, H. D. Hinton, and J. A. Nieuwland, *ibid.*, 1932, **54**, 3694.

²⁹ *Eidem*, *ibid.*, 1933, **55**, 3402.

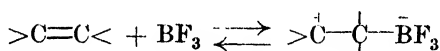
³⁰ W. J. Croxall, F. J. Sowa, and J. A. Nieuwland, *ibid.*, 1934, **56**, 2054; 1935, **57**, 1549.

by rearrangement), and under the influence of the same catalyst, benzene³¹ and naphthalene³² have been alkylated by alcohols; esters³³ and ethers³⁴ can also alkylate. The Claisen rearrangement of phenolic ethers, which is catalysed by boron fluoride, aluminium chloride and other agents, is probably an intermolecular process involving nuclear alkylation,³⁵ and the Fries rearrangement similarly involves acylation. Other reactions which are catalysed by boron fluoride include the addition of alcohols to acetylene to give acetals,²¹ and the preparation of phenolphthalein and fluorescein.³⁶

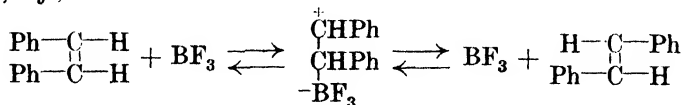
The view that alcohols, esters and ethers are first converted into olefin, which is the active agent in alkylations,^{31, 33, 34} has been shown to be untenable³² on the following grounds: (a) although cyclohexanol alkylates naphthalene in presence of boron fluoride, the alcohol can be recovered unchanged after treatment with the catalyst under conditions more drastic than those required for alkylation, and (b) olefin formation is not possible from benzyl alcohol, which nevertheless alkylates.³⁷ Price and Ciskowski therefore suggest that a carbonium ion is the active intermediate, *e.g.*,



where R = alkyl and R' = alkyl or acyl. A similar mechanism is suggested for alkylation by olefins and for the catalysed polymerisation of olefins, the first step being



C. C. Price and M. Meister³⁸ consider that the catalysis of geometrical inversion depends upon the co-ordination of the catalyst (*e.g.*, BF_3) at one of the unsaturated carbon atoms, the freedom of rotation consequent upon the transformation of the olefinic linkage to a single bond making the inversion possible, *e.g.*,



It may be noted, however, that the occurrence of the hydron-catalysed change of maleic into fumaric acid in this way is unlikely, since the presence of deuterium chloride does not lead to a product containing deuterium,³⁹

³¹ J. F. McKenna and F. J. Sowa, *J. Amer. Chem. Soc.*, 1937, **59**, 470; N. F. Toussaint and G. F. Hennion, *ibid.*, 1940, **62**, 1145.

³² C. C. Price and J. M. Ciskowski, *ibid.*, 1938, **60**, 2499.

³³ J. F. McKenna and F. J. Sowa, *ibid.*, 1937, **59**, 1204.

³⁴ M. J. O'Connor and F. J. Sowa, *ibid.*, 1938, **60**, 125; A. J. Kolka and R. R. Vogt, *ibid.*, 1939, **61**, 1463.

³⁵ See *Ann. Reports*, 1939, **36**, 208.

³⁶ J. F. McKenna and F. J. Sowa, *J. Amer. Chem. Soc.*, 1938, **60**, 124.

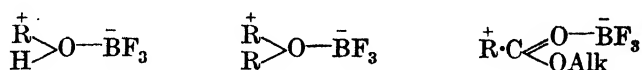
³⁷ Compare E. Bowden, *ibid.*, p. 645. ³⁸ *Ibid.*, 1939, **61**, 1595.

³⁹ C. Horrex, *Trans. Faraday Soc.*, 1937, **33**, 570.

and K. Nozaki and R. Ogg⁴⁰ have put forward a mechanism in which the acid catalyst here co-ordinates at oxygen of carboxyl, and anions, which also appear to play a part, may become attached at one of the olefinic carbon atoms; inversion under the influence of amines is represented similarly.⁴¹

The catalytic effects of boron fluoride and aluminium chloride must, of course, be dependent upon the ability of these molecules to accept an electron pair, and the resulting production of alkyl ions is in harmony with the strongly acidic qualities of BF_3 -alcohol complexes.²¹ The existence of an ionised complex at an intermediate stage in the familiar Friedel-Crafts reactions involving alkyl halides has frequently been postulated, and is rendered more probable by the work of E. Wertyporoch and of F. Fairbrother.⁴² Fairbrother has shown recently that, for a number of pairs of inorganic and organic bromides, the ease of exchange of radioactive bromine is closely parallel to the reactivity in the Friedel-Crafts synthesis, and the formation of highly polar complexes is indicated by dielectric-constant measurements.⁴³ The "activation" of the alkyl halide, alcohol, ether, ester or olefin by the catalyst must consist fundamentally in its conversion into a complex which is a strongly electrophilic reagent, for (a) the orientation of nuclear alkylation is, with certain exceptions, the same as in nuclear halogenation, nitration and sulphonation, and (b) alkylation of a nucleus already containing a powerfully activating group such as hydroxyl may occur in presence of a less powerful catalyst, and a reagent such as benzyl chloride which is already strongly electrophilic owing to the facility of

ionisation, $\text{Ph}\cdot\text{CH}_2\text{---}\overset{\curvearrowright}{\text{Cl}}$, can alkylate in absence of a catalyst. The co-ordination compounds of boron fluoride with alcohols, ethers and esters may be represented as follows :



which means probably that ionised structures in which R^+ is dissociated from the remainder of the molecule participate in the mesomeric state. This accounts for the observation that a normal alkyl group of more than two carbon atoms usually isomerises (e.g., $\text{CH}_3\cdot\text{CH}_2\cdot\text{CH}_2$ will exist as

$\text{CH}_3\cdot\overset{+}{\text{CH}}\cdot\text{CH}_2$). In the case of an olefin, the alkylating agent is no doubt

that formulated by Price and Ciskowski, and it is easy to understand why, for example, propylene introduces an *isopropyl* group *via* the complex $\text{CH}_3\cdot\overset{+}{\text{CH}}\cdot\text{CH}_2\text{---}\bar{\text{B}}\text{F}_3$. The co-ordination complex of aluminium chloride

⁴⁰ *J. Amer. Chem. Soc.*, 1941, **63**, 2583.

⁴¹ *Ibid.*, p. 2681.

⁴² See *Ann. Reports*, 1937, **34**, 252. V. N. Ipatieff, H. Pines, and L. Schmerling (*J. Org. Chem.*, 1940, **5**, 253) include similar complexes in their alkylation mechanisms; they also discuss the isomerisation of groups.

⁴³ *J.*, 1941, 293; *Trans. Faraday Soc.*, 1941, **37**, 763.

with an alkyl halide will be $R-X \rightarrow AlCl_3$, which will give rise to ionised structures such as $[R-X-AlCl_2 \ Cl^-]$, $[R^+ \ XAlCl_3]$, $[R^+ \ XAlCl_2 \ Cl^-]$, and $[R^+ \ AlCl_3 \ X^-]$; the participation of $[R^+ \ AlCl_3 \ X^-]$ accounts for the equivalence of the four halogen atoms observed by Fairbrother.⁴² Since boron fluoride apparently does not catalyse alkylation by alkyl halides, the structures in which the alkyl group is ionised may not be of much importance in the

complex $R-X \rightarrow BF_3$, i.e., the process $R-X \rightarrow BF_3$ does not occur sufficiently to render the complex strongly electrophilic. The entry of a second alkyl group into the *m*-position has been ascribed to the reversibility of the Friedel-Crafts reaction, the 1 : 2 : 4-trialkylated compound being formed and the 1-alkyl group then expelled.

The view that the alkylating agent is a carbonium ion (or a mesomeric form in which ionised structures participate to an important extent) appears at first sight to be at variance with Hickinbottom's view that, in the Claisen rearrangement, the group migrates as a neutral radical.⁴⁴ This view is based, however, upon observations of the rearrangement brought about by heat alone, and the mechanism of the catalysed change is not necessarily the same.

(b) Rearrangements.

(Continued from *Ann. Reports*, 1939, 36, 191.)

Continuing previous work in which optically active hydratropamide, $CHPhMe \cdot CO \cdot NH_2$, was shown to be converted into α -phenylethylamine with a 95.8% retention of optical activity,⁴⁵ J. Kenyon and D. P. Young⁴⁶ find that the Curtius degradation of hydratropic azide gives an amine of 99.3% optical purity. The intramolecular character of the Curtius change is thus confirmed. The authors suggest that the loss of optical activity observed in the Hofmann rearrangement of the amide, which, though small, is real, may be attributed to some racemisation of the intermediate isocyanate, a view which is based upon an earlier observation by E. S. Wallis and R. D. Dripps,⁴⁷ who found that an optically active isocyanate is racemised on alkaline hydrolysis (as in the Hofmann change) but not on acid hydrolysis (as in the Curtius reaction). The intramolecular nature of the Beckmann transformation is demonstrated by the retention of optical activity in the conversion of methyl γ -heptyl ketoxime into aceto- γ -heptylamide. Kenyon and Young point out that an optically active radical which is transferred in a Hofmann, Curtius or Beckmann change retains not only its asymmetry but also its configuration, i.e., no Walden inversion occurs. This was formerly assumed,⁴⁸ and P. D. Bartlett and L. H. Knox⁴⁹ showed that the Hofmann rearrangement could occur in a case where inversion was not possible. Direct evidence of the absence of optical

⁴⁴ See *Ann. Reports*, 1939, 36, 209.

⁴⁵ *Ibid.*, p. 193.

⁴⁶ *J.*, 1941, 263.

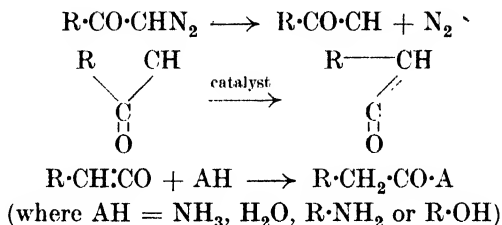
⁴⁷ *J. Amer. Chem. Soc.*, 1933, 55, 1701.

⁴⁸ E. S. Wallis and S. C. Nagel, *ibid.*, 1931, 53, 2787; J. von Braun and E. Friehmelt, *Ber.*, 1933, 66, 684.

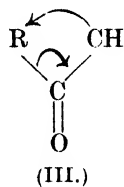
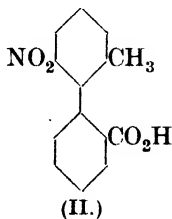
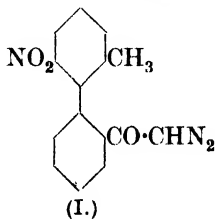
⁴⁹ *J. Amer. Chem. Soc.*, 1939, 61, 3184.

inversion in the Hofmann rearrangement is provided by some earlier results of W. A. Noyes and co-workers,⁵⁰ who converted the half amide of camphoric acid into the corresponding amino-acid without inversion, and the proof of the identity in configuration between benzylmethylacetic acid and α -benzylethylamine hydrochloride of the same sign of rotation⁵¹ together with the conversion of the former into the latter *via* the amide or the azide⁵² gives another demonstration.

The stereochemical method has also been used in J. F. Lane and E. S. Wallis's study⁵³ of the Wolff rearrangement of diazo-ketones, which occurs when these compounds are treated with ammoniacal silver nitrate and certain other reagents. The mechanism suggested some time ago by B. Eistert⁵⁴ is as follows :



A case of this rearrangement without accompanying racemisation had been reported at an earlier date,⁵⁵ and in order to obtain further evidence of its intramolecular character Lane and Wallis rearranged the diazo-ketone CMeBuPh \cdot CO \cdot CHN₂ in boiling aniline and also in aqueous dioxan containing silver oxide and sodium thiosulphate; in neither case did the optically active diazo-ketone give a racemic product. The compound (I) was submitted to the same treatment, this substance being chosen because F. Bell had previously shown that when optically active specimens of the acid (II) are degraded by either the Hofmann or the Curtius reaction the resulting amine is active;⁵⁶ again no racemisation was observed. It is concluded that here, as in the Hofmann and the Curtius change, the group is never released, and it would appear that the Wolff rearrangement is quite similar to these degradations, being represented most probably as in (III).⁵⁷



⁵⁰ See S. Archer, *J. Amer. Chem. Soc.*, 1940, **62**, 1872.

⁵¹ J. Kenyon, H. Phillips, and (Miss) V. P. Pittman, *J.*, 1935, 1072.

⁵² E. S. Wallis *et al.* See *Ann. Reports*, 1939, **36**, 193.

⁵³ *J. Org. Chem.*, 1941, **6**, 443.

⁵⁴ *Ber.*, 1935, **68**, 208.

⁵⁵ N. A. Preobrashenski, A. M. Poljakova, and V. A. Preobrashenski, *ibid.*, p. 850.

⁵⁶ *J.*, 1934, 836.

⁵⁷ Compare *Ann. Reports*, 1939, **36**, 194.

Optically active benzylmethyldiazoacetone, $\text{CH}_2\text{Ph}\cdot\text{CHMe}\cdot\text{CO}\cdot\text{CHN}_2$, however, rearranges to give a partially or completely racemised product⁵⁸ and it is suggested that this may be due to the presence of an enolisable hydrogen.

The catalytic effect of phenols on the Wagner-Meerwein rearrangement has been discussed by P. D. Bartlett and J. D. Gill.⁵⁹ They find that the efficiencies of four phenols as catalysts of the change of camphene hydrochloride into *isobornyl* chloride stand in the order of their hydrogen-bonding powers, and conclude that the phenol solvates the chloride ion; the variation of the reaction rate with the concentration of the phenol indicates that the attack takes place in two ways, involving one and two molecules of the phenol.

It is interesting that F. C. Whitmore, A. H. Popkin, H. I. Bernstein, and J. P. Wilkins⁶⁰ were unable to isolate any *tert.*-amyl derivatives from the products of the action of metallic sodium upon *neopentyl* chloride; the Wurtz reaction proceeds *via* free radicals,⁶¹ and it appears that under conditions giving radicals the *neopentyl* group does not undergo the change to *tert.*-amyl which occurs in processes where it appears as a positive ion.

A few studies of certain migrations, from the side chain to the nucleus of aromatic compounds have been recorded since the Annual Report for 1939. P. J. Drumm, W. F. O'Connor, and J. Reilly⁶² have examined the products of the Hofmann-Martius rearrangement of dibenzylaniline hydrochloride, and find *p*-aminodiphenylmethane, 1-amino-2 : 4-dibenzylbenzene and also an aminotribenzylbenzene, probably the 2 : 4 : 6-compound; this appears to be the first example of the introduction of more than two groups by this reaction. The electronic mechanism of the benzidine transformation has been discussed by Sir R. Robinson in his Presidential Address to the Chemical Society,⁶³ and E. D. Hughes and C. K. Ingold⁶⁴ have published some comments on this reaction. A summary of our knowledge of the Fries reaction, with a discussion of proposed mechanisms, has appeared.⁶⁵ A. W. Ralston, M. R. McCorkle, and S. T. Bauer⁶⁶ find that variations in the quantity of aluminium chloride and in the solvent influence the *o/p* ratio in the Fries rearrangement and in the Friedel-Crafts reaction similarly, indicating an analogy between the two processes.

D. S. Tarbell and J. F. Kincaid⁶⁷ have shown that the Claisen rearrangement of 2 : 6-dimethylphenyl allyl ether to 2 : 6-dimethyl-4-allylphenol is kinetically unimolecular. There is further evidence that in the *p*-rearrangement the α -carbon, and not the γ -carbon as in the *o*-rearrangement of aryl allyl ethers, becomes linked to the nucleus,⁶⁸ and stereochemical considerations indicate that the former change must be intermolecular. Neverthe-

⁵⁸ J. F. Lane, J. Willenz, A. Weissberger, and E. S. Wallis, *J. Org. Chem.*, 1940, 5, 276.

⁵⁹ *J. Amer. Chem. Soc.*, 1941, 63, 1273.

⁶⁰ *Ibid.*, p. 124.

⁶¹ See *Ann. Reports*, 1940, 37, 286.

⁶² *J. Amer. Chem. Soc.*, 1940, 62, 1241.

⁶³ *J.*, 1941, 220.

⁶⁴ *Ibid.*, p. 608.

⁶⁵ A. H. Blatt, *Chem. Reviews*, 1940, 27, 413.

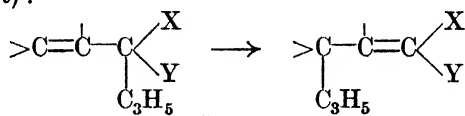
⁶⁶ *J. Org. Chem.*, 1940, 5, 645.

⁶⁷ *J. Amer. Chem. Soc.*, 1940, 62, 728.

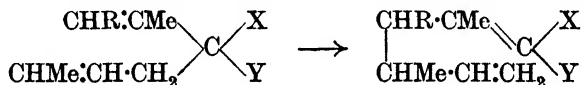
⁶⁸ O. Mumm and J. Diederichsen, *Ber.*, 1939, 72, 1523; E. Späth and F. Kuffner, *ibid.*, p. 1580.

less, W. I. Gilbert and E. S. Wallis⁶⁹ detected no migration of a group to a foreign nucleus when phenyl isopropyl ether and *p*-tolyl *sec*-butyl ether were rearranged in the same solution in presence of sulphuric acid, and they conclude that the mobile group is at all times within the sphere of influence of the molecule. There are instances, however, where this group has been found linked to another molecule.⁷⁰ A comprehensive account of the facts relating to the Claisen rearrangement has been published by D. S. Tarbell.⁷¹

Compounds such as vinyl allyl ether, which contain the essential part of the aryl allyl ether skeleton, undergo a change exactly similar to the Claisen rearrangement, and an analogous change in certain three-carbon systems has now been discovered by A. C. Cope and co-workers.⁷² On heating to temperatures between 135° and 200° the following occurs (X and Y = CN or CO₂Et):



The rearrangement becomes less easy in the order malonitriles > cyano-acetic esters > malonic esters, and is kinetically unimolecular. In the rearrangement of the related crotyl compounds, it has been shown that the migrating group becomes linked through the γ -carbon atom; e.g.,



and if two esters containing severally allyl and crotyl groups are rearranged together, no interchange of migrating groups occurs. There can therefore be little doubt that the change is intramolecular.

(c) *The ortho-Effect; Steric Inhibition of Mesomerism.*

(Continued from *Annual Reports*, 1939, **36**, 215.)

A reduction of the mesomeric effects of the nitro- and dimethylamino-groups by two methyl groups standing in *o*-positions with respect to them, as in dimethylmesidine, nitrodurene and nitrodimethylaminodurene, was postulated by Hampson and co-workers⁷³ in their discussion of the dipole moments of these compounds, which are considerably lower than those of the corresponding compounds in which the methyl groups are absent; it was considered that the *o*-methyl groups would make it difficult for the NO₂ or NMe₂ to come into the plane of the nucleus, thus producing conditions unfavourable to mesomerism. The study of cases of this kind has now been extended, particularly by workers at the University of Chicago. R. G. Kadesch and S. W. Weller⁷⁴ find that the dipole moments of acetylmesitylene (2.71D.) and acetyldurene (2.68) are almost identical with those of aliphatic

⁶⁹ *J. Org. Chem.*, 1940, **5**, 184.

⁷⁰ See *Ann. Reports*, 1939, **36**, 207.

⁷¹ *Chem. Reviews*, 1940, **27**, 495.

⁷² *J. Amer. Chem. Soc.*, 1940, **62**, 441; 1941, **63**, 1843, 1852.

⁷³ *J.*, 1937, 10; 1939, 981.

⁷⁴ *J. Amer. Chem. Soc.*, 1941, **63**, 1310.

ketones, and suppose that the *o*-methyl groups inhibit the mesomeric effect of the carbonyl group which operates in acetophenone ($\mu = 2.88$); observations of the absorption spectra of acetylmesitylene and 2 : 4 : 6-triisopropylacetophenone point to the same conclusion.⁷⁵ On the other hand, *o*-methyl groups produce no diminution of the moment of benzaldehyde (2.92; μ for mesitylaldehyde = 2.96), and models show that, whereas these groups interfere very considerably with methyl of the $\text{CO}\cdot\text{CH}_3$ in acetophenone, any such interference with the hydrogen of the aldehyde is almost negligible. The moment of 2 : 4 : 6-trimethylbenzoyl chloride (2.95), again, is appreciably less than that of the unsubstituted acid chloride (3.32).

Hampson's conception of a steric inhibition of mesomerism has stimulated interest in the chemical aspects of the "*ortho*-effect," and was adopted by G. Baddeley⁷⁶ as the basis of the interpretation of a number of the peculiarities associated with compounds in which two groups stand in *o*-positions with respect to each other. An inhibition of mesomerism is also postulated by G. W. Wheland and A. A. Danish⁷⁷ in order to explain the reduction of the acidic character of 4 : 4' : 4''-trinitrotriphenylmethane by methyl groups in the six positions *ortho* to the nitro-groups. R. T. Arnold, G. Peirce, and R. A. Barnes⁷⁸ find, too, that 4-nitrodimethyl- α -naphthylamine is a much stronger base than 4-nitro- α -naphthylamine, and they suppose that the interference of the second ring with the bulky dimethylamino-group here renders it difficult or impossible for this group to become coplanar with the nucleus, thus reducing the mesomerism with a consequent increase in basic strength; confirmation is found in the lower melting points of the *N*-dialkyl compounds as compared with the primary amine ($\text{R}\cdot\text{NH}_2$, 191°. $\text{R}\cdot\text{NMe}_2$, 65°. $\text{R}\cdot\text{NEt}_2$, liquid), which indicate a less polar character. On the other hand, R. D. Kleene, F. H. Westheimer, and G. W. Wheland⁷⁹ have observed that the relative strengths of substituted *cis*- and *trans*-cinnamic acids cannot be accounted for on the basis of the steric inhibition of mesomerism; for instance, the dissociation constant (in 40% acetone) of *trans*-2 : 4 : 6-trimethylcinnamic acid is greater by a factor of 2.5 than that of the *cis*-isomeride, although the former is probably planar whereas the latter is certainly not.

From measurements of the reactions of piperidine with some nitro- and cyano-bromobenzenes, W. C. Spitzer and G. W. Wheland⁸⁰ conclude that mesomerism can be inhibited in suitably substituted aromatic nitro-compounds but not in the corresponding cyano-derivatives, although in the former case the effect is smaller than would be expected from the dipole-moment measurements of R. H. Birtles and G. C. Hampson.⁷³ F. H. Westheimer and R. P. Metcalf's study of the alkaline hydrolysis of a number of substituted ethyl benzoates having NO_2 , NH_2 or NMe_2 in the *p*-position⁸¹ has shown that the effects of these groups (of which NO_2 accelerates and the others retard the reaction) are rendered smaller by methyl groups at the

⁷⁵ M. T. O'Shaughnessy and W. H. Rodebush, *J. Amer. Chem. Soc.*, 1940, **62**, 2906.

⁷⁶ *Nature*, 1939, **144**, 444.

⁷⁸ *Ibid.*, p. 1627.

⁸⁰ *Ibid.*, 1940, **62**, 2995.

⁷⁷ *J. Amer. Chem. Soc.*, 1940, **62**, 1125.

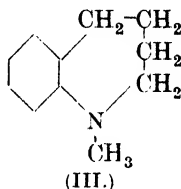
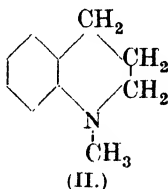
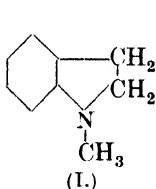
⁷⁹ *Ibid.*, 1941, **63**, 791.

⁸¹ *Ibid.*, 1941, **63**, 1339.

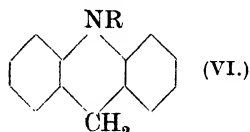
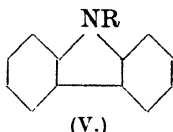
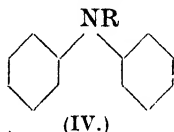
3 : 5-positions; this is particularly striking in the case of ethyl 4-dimethyl-amino-3 : 5-dimethylbenzoate, as illustrated by the velocity coefficients below :

at 30°	ethyl benzoate	0.052	} Ratio
	ethyl 4-dimethylaminobenzoate	0.00152	
at 55°	ethyl 3 : 5-dimethylbenzoate	0.373	} Ratio
	ethyl 4-dimethylamino-3 : 5-dimethylbenzoate	0.206	

A reduction in the reactivity of the *p*-position owing to the presence of a group placed *ortho* to NMe_2 was observed by von Braun in 1916,⁸² and in an investigation of the deuteration of derivatives of dimethylaniline, W. G. Brown, A. H. Widiger, and N. J. Letang⁸³ find a similar effect in *o*-bromo- and *o*-chloro-dimethylaniline, but very little in the *o*-fluoro-compound. When the nitrogen is linked to the *ortho*-carbon atom to form a five-, six- or seven-membered ring system, as in *N*-methylindoline (I), *N*-methyl-tetrahydroquinoline (II), and *N*-methylhomotetrahydroquinoline (III), however, the reactivity is dependent upon the size of the second ring; in (I) and (II), where it is coplanar with the benzene ring (or almost so), the reactivity is high, exceeding that in dimethylaniline itself, but the puckered seven-membered ring in (III) leads to a relatively slow reaction.



The authors consider that " these results provide rather convincing evidence that the key to the situation really lies in the ability of the dialkylamino-group to come into the plane of the benzene ring "; *i.e.*, the mesomeric (and, in a reaction, the electromeric) effect of the group is inhibited when it is not able to do so. In a recent paper,⁸⁴ Brown and Letang have demonstrated a reduction of reactivity (in the deuteration reaction) in dimethyl- α -naphthylamine by chlorine or a nitro-group in the 8-position, and also a mutual hindrance of dimethylamino-groups in the *peri*-positions. Extension of this work to carbazole derivatives (V), however, has given results which are



less easy to interpret, for these compounds are less reactive than the corresponding diphenylamine derivatives (IV) in spite of their favourable planar structure. Dihydroacridine derivatives (VI) also show a depression of

⁸² See *Ann. Reports*, 1939, **36**, 218.

⁸³ *J. Amer. Chem. Soc.*, 1939, **61**, 2597.

⁸⁴ *Ibid.*, 1941, **63**, 358.

reactivity as compared with (IV), but this may be due to a folded structure similar to that of dihydroanthracene and *NN'*-dimethyldihydrophenazine.⁸⁵

These new results appear to confirm the suggestion made in the *Annual Reports* for 1939 that the various manifestations of the "*ortho*-effect" cannot be interpreted on the basis of a single conception; steric inhibition of mesomerism, interaction between groups in *o*-positions, and perhaps also geometrical steric hindrance as envisaged by Victor Meyer will probably all find their place in a final and comprehensive interpretation of the observed phenomena when such an interpretation is achieved.

H. B. W.

(d) *The Strengths of Organic Acids and Bases.*

The classical dissociation constants of Wilhelm Ostwald provided the earliest numerical data which reflected the changes in reactivity attendant upon systematic variations in chemical structure, and the rise of the theory of interionic attraction has led more recently to the computation of thermodynamic dissociation constants (*K*) which furnish a better measure of the strengths of organic acids than do the older values. The later data are superior not only because the corrections made necessary by modern theory are taken into account in their derivation, but also by reason of improvements in experimental technique. Wide use has been made of the dissociation constants for aqueous solution in discussion of the polar influences of substituent groups, and several investigators have been able to relate them quantitatively with reactivities and other characteristics of organic molecules.^{1,2} A collection of the more reliable dissociation constants of monobasic organic acids and the strengths of organic bases (for one temperature) has been published recently,³ and to this may now be added further values for formic, *n*-butyric and cyanoacetic acids.⁴

Most of the available data relate to aqueous solution at 25°, and quite recently doubts have been expressed as to the correctness of basing comparisons of acid strengths upon the values of dissociation constants for an arbitrarily fixed temperature and a single selected solvent.

The factors governing acid dissociation will be affected by elevation of temperature, both the solvent and the electrolyte being directly concerned. The dielectric constant of a liquid diminishes with increasing temperature, and so with the decreasing electric field there will be a smaller tendency for ions to separate. Again, there is less solvation and also loss of complexity in both solute and solvent.

There exist comparatively few data relating to the variation of dissociation constants of organic acids with temperature, and those of a reliable

⁸⁵ (Miss) I. G. M. Campbell, (Mrs.) C. G. Le Fèvre, R. J. W. Le Fèvre, and E. E. Turner, *J.*, 1938, 404.

¹ See *Ann. Reports*, 1937, **34**, 52; 1938, **35**, 239; 1939, **36**, 215.

² H. O. Jenkins, *J.*, 1940, 1447.

³ J. F. J. Dippy, *Chem. Reviews*, 1939, **25**, 151.

⁴ B. Sexton and L. S. Darken, *J. Amer. Chem. Soc.*, 1940, **62**, 846.

character are still further limited.* The last-mentioned refer in the main to some common monocarboxylic acids (including ampholytes), mostly in aqueous solution over a temperature range of usually 0—60° (determined largely by the e.m.f. method perfected by Harned), although some measurements on partially aqueous solutions have been performed.

It is plain from the available values that the dissociation constants of uncharged acids pass through maxima with rise of temperature, and various attempts to relate K with temperature have been made with acids of this charge type. In the first place Harned and co-workers⁸ fitted their earlier results to the four-constant equation,

$$\log K = -a/T + b \log T + cT + d \quad . \quad . \quad . \quad (1)$$

where T is the temperature in degrees absolute. This they replaced later by a further empirical equation,⁹ for temperatures in the vicinity of the maximum, which has the general form,

$$\log K - \log K_m = -p(t - \theta)^2 \quad . \quad . \quad . \quad (2)$$

where K_m is the maximum dissociation constant, θ the corresponding temperature (°C), K the dissociation constant at some other temperature t (°C), and p a constant.¹⁰ An excellent account of the applicability of this equation to the experimental data has been published by H. S. Harned and B. B. Owen,⁵ and a qualitative interpretation provided by R. W. Gurney.¹¹ Since then a relationship arising from theoretical treatment, and applicable, like equation (2), in the neighbourhood of K_m , has been put forward by J. L. Magee, T. Ri, and H. Eyring,¹² viz.,

$$\ln K - \ln K_m = p(t - \theta)^2 + q(t - \theta)^3 + \quad . \quad . \quad . \quad (3)$$

in which the constants p and q are dependent largely on the properties of the solvent, in the case of water. This is similar to equation (2) apart from the cubic and higher terms; the inclusion of the cubic term leads to a slightly different curve in the plot of $\log K$ against t , which the authors consider to fit the experimental points better.

* These have been listed by :

⁵ H. S. Harned and B. B. Owen, *Chem. Reviews*, 1939, **25**, 31.

⁶ D. H. Everett and W. F. K. Wynne-Jones, *Trans. Faraday Soc.*, 1939, **35**, 1380.

⁷ J. F. J. Dippy and H. O. Jenkins, *ibid.*, 1941, **37**, 366.

Additional measurements have lately been provided by : W. F. K. Wynne-Jones and G. Salomon, *ibid.*, 1938, **34**, 1321; H. S. Harned, *J. Physical Chem.*, 1939, **43**, 275; H. Suter and K. Lutz, *Helv. Chim. Acta*, 1940, **23**, 1191; J. E. Ablard, D. S. McKinney, and J. C. Warner, *J. Amer. Chem. Soc.*, 1940, **62**, 2181; F. C. Hickey, *ibid.*, p. 2916; D. H. Everett and W. F. K. Wynne-Jones, *Proc. Roy. Soc.*, 1941, **A**, **177**, 499; J. H. Elliott and M. Kilpatrick, *J. Physical Chem.*, 1941, **45**, 466; H. S. Harned and R. S. Done, *J. Amer. Chem. Soc.*, 1941, **63**, 2579.

⁸ H. S. Harned and R. W. Ehlers, *J. Amer. Chem. Soc.*, 1933, **55**, 2379.

⁹ H. S. Harned and N. D. Embree, *ibid.*, 1934, **56**, 1050.

¹⁰ See *Ann. Reports*, 1937, **34**, 101—105.

¹¹ *J. Chem. Physics*, 1938, **6**, 499.

¹² *Ibid.*, 1941, **9**, 419.

K. S. Pitzer¹³ has claimed superiority for the equation

$$\ln K = \frac{A}{T} + B + \frac{\Delta C_p \ln T}{R} \quad . \quad . \quad . \quad (4)$$

(where A and B are constants) in that it has wider applicability, although it is agreed that, within limits, this is essentially the same as the Harned and Embree relationship. In this equation Pitzer assumes for the fatty acids a value of -40 cal./degree for ΔC_p , the heat capacity change, invariant with respect to temperature within the experimental range.

D. H. Everett and W. F. K. Wynne-Jones⁶ propose the equation

$$\ln K = -\frac{\Delta H_0}{RT} + \frac{\Delta C_p \ln T}{T} + \frac{(\Delta S_0^\circ - \Delta C_p)}{R} \quad . \quad . \quad . \quad (5)$$

which they believe to be an improvement on others; this is similar to Pitzer's equation except that significance is given to constants A and B . The quantities ΔH_0 , ΔS_0° and ΔC_p (the heat and entropy of ionisation at absolute zero and the change of heat capacity at constant pressure, respectively) are considered to be unaffected by temperature. It has been pointed out,⁷ however, that the temperature invariance of ΔC_p in chemical reactions has certainly not been proved, and such an assumption is, at best, an approximation applying over a very limited temperature range.

In a review of the position, H. S. Harned and R. A. Robinson¹⁴ have compared equation (2) with three other equations, all considered likely to account for change of K with temperature [one being essentially that proposed by Everett and Wynne-Jones, *i.e.*, equation (5)]. They conclude that, whereas the Harned-Embree expression is only a first approximation, the other three equations are all capable of representing the data within the limits of experimental accuracy, and state that on the present evidence they are of equal merit. It is emphasised by Harned and Robinson that experiments over the present limited temperature ranges fail to decide whether or not ΔC_p is independent of temperature, because, although the three equations mentioned seem to be of equal applicability, two of them predict a heat capacity term proportional to the temperature, whilst according to the other equation (that of the form proposed by Everett and Wynne-Jones) it is independent of temperature. For practical purposes Harned and Robinson decide in favour of the equation which lends itself best to calculation, and thus the dissociation constant is expressed as

$$\log K = -A/T + B - CT \quad . \quad . \quad . \quad (6)$$

where A , B and C are empirical constants derived from the experimental data.¹⁵ H. S. Harned and R. S. Done¹⁶ have lately shown that this equation represents well their observed values of K for formic acid in four water-dioxan mixtures at temperatures ranging from 0° to 50° .*

¹³ *J. Amer. Chem. Soc.*, 1937, **59**, 2385. ¹⁴ *Trans. Faraday Soc.*, 1940, **36**, 973.

¹⁵ Compare with the equation of F. C. Baughan (*J. Chem. Physics*, 1939, **7**, 951).

¹⁶ *J. Amer. Chem. Soc.*, 1941, **63**, 2579.

* H. S. Harned and T. R. Dedell (*J. Amer. Chem. Soc.*, 1941, **63**, 3308) have since shown that the ionisation constants of acetic and propionic acids in dioxan-water mixtures can also be expressed by the Harned-Robinson equation.

At the present time, therefore, there exist a number of different equations, embodying by no means identical premises, but all capable of accounting reasonably well for the experimental facts; their reliability for extrapolation purposes is uncertain, however. This forms the basis of a criticism ⁷ of Everett and Wynne-Jones's use of the values of ΔH_0 as representing the relative "intrinsic strengths" of series of acids. Thus, it is contended that the order of strengths *n*-butyric > propionic > acetic > formic, arrived at by these authors, is opposed to the abundant evidence from other fields of inquiry [which shows that alkyl attached to carbon is electron-repulsive (+ *I*, + *M*)], and that it is probably the outcome of unjustifiable extrapolation. It is evident, nevertheless, that in the case of *n*-butyric acid the curve obtained by plotting log *K* against *t* is displaced with respect to the curves for the other aliphatic acids so far studied,* and that, as a consequence the strengths of the simpler fatty acids might not present the same sequence at all temperatures.† This anomaly is identified with a suggested restricting potential arising from an attraction between the C—CH₃ and C=O dipoles (hydrogen-bonding), particularly in the anion.¹⁷ Independent evidence favouring this suggestion has been supplied by J. P. McKeynolds and J. R. Witmeyer¹⁸ in a study of the stabilities to racemisation of certain salts containing aliphatic acid radicals. Also, Magee, Ri, and Eyring,¹² discussing the enhanced *K* for *n*-butyric acid at 25°, indicate that for a regular gradation of dissociation constants in the fatty series the heat of ionisation of *n*-butyric acid would be about - 250 cal., and not - 691 cal., and they give the postulated hydrogen-bonding as the probable reason for this large value. It appears probable, therefore, that the dissociation constants of the simple fatty acids at any fixed temperature will present an order which is consistent with the known influences of alkyl groups, provided that allowance is made for an additional spatial interaction in *n*-butyric acid and higher acids. The use of ΔH_0 as a measure of true acid strength seems to apply no more successfully in the benzoic acid series, where it leads to a number of conclusions which conflict with the well-defined polar effects of substituents such as iodine and nitroxyl.

Another basis of comparing acid strengths, regarded as less arbitrary than the use of dissociation constants at some fixed temperature, has been proposed by Harned and Embree.⁹ They recommend that the values of

¹⁷ J. F. J. Dippy, *J.*, 1938, 1222; H. O. Jenkins and J. F. J. Dippy, *J. Amer. Chem. Soc.*, 1940, **62**, 483; see *Ann. Reports*, 1938, **35**, 251.

¹⁸ *J. Amer. Chem. Soc.*, 1940, **62**, 3148.

* R. W. Gurney (ref. 11) has already indicated that there is no correlation between the degree of dissociation of an acid and the value of θ . He regards the value of the latter as dependent on the relative magnitudes of the electrostatic and non-electrostatic parts of the dissociation energy. See also Everett and Wynne-Jones (ref. 6).

† Only in the cases of ampholytes have different sequences of acid strength been obtained in practice by varying the temperature (compare J. F. J. Dippy and H. O. Jenkins, ref. 7, and D. H. Everett and W. F. K. Wynne-Jones, *Trans. Faraday Soc.*, 1941, **38**, 374), although it is not certain to what extent this is accounted for by constitutional changes.

dissociation constants at their maxima (*i.e.*, where ΔH is zero) should be selected. It seems, however, on examination of the available data (excluding ampholytes), that no different sequence of strengths is exhibited where this method of comparison is adopted.¹⁹ Everett and Wynne-Jones consider that this method is inadequate.

L. P. Hammett²⁰ has called attention to the fact that different conclusions regarding the influences of substituent groups would be derived from consideration of heats of ionisation ($\Delta H = RT^2 d \ln K/dT$) on the one hand, and free energies of ionisation ($\Delta F = -RT \ln K$) on the other, since the effect of a substituent on the two quantities is far from comparable. It is clear, however, that values for the free energy change can be ascertained with much the greater certainty, and actually ΔF does represent the maximum work which the system is capable of performing. In this connexion it is noteworthy that Harned and Done,¹⁶ in an estimate of the accuracy of the determinations of the thermodynamic functions evaluated from dissociation constant-temperature data, emphasise that the value of the heat of ionisation is subject to large errors because of the difficulty of determining a quantity by differentiation.

It is significant, however, that J. G. Kirkwood, F. H. Westheimer, and collaborators²¹ have successfully elaborated N. Bjerrum's original proposition²² that the effect on K due to the introduction of a polar substituent into an organic acid is primarily electrostatic in origin. On this basis, the ratio of the strengths of two acids has been calculated from the electrostatic work done in transferring a proton from one acid to the anion of the other; the formulation takes into account the position of the substituent and the shape of the molecule. Monobasic and dibasic aliphatic and monobasic aromatic acids and certain phenols have been examined, and, on the whole, a close correspondence between predicted and observed strengths has been noted. A similar fundamental assumption is implicit in H. O. Jenkins's correlations.¹

In short, the foregoing criticisms have to contend with the fact that dissociation constants for a fixed temperature display pronounced regularities which are in harmony with a mass of observations proceeding from other investigations, and that such agreement would scarcely have existed unless the method of comparing acid and base strengths was, in the main, a good approximation to the truth.

There remains the question as to whether identical conclusions would be reached regarding the relative polar effects of substituent groups if data for organic acids in solvents other than water were taken into account. It was indicated by W. F. K. Wynne-Jones²³ that examination of the data for a collection of acids in alcohols and water showed differing orders of strengths,

¹⁹ See J. F. J. Dippy, *J.*, 1938, 1222.

²⁰ *J. Chem. Physics*, 1936, 4, 613.

²¹ *Ibid.*, 1938, 6, 507, 513; *J. Amer. Chem. Soc.*, 1939, 61, 555, 1977; compare A. Eucken, *Angew. Chem.*, 1932, 45, 203; G. Schwarzenbach and H. Egli, *Helv. Chim. Acta*, 1934, 7, 1183.

²² *Z. physikal. Chem.*, 1923, 106, 219.

²³ *Chem. and Ind.*, 1933, 52, 273.

but G. N. Burkhardt²⁴ pointed out that the irregularities were due to the inclusion of certain acids already recognised as exhibiting abnormally high strengths. Nevertheless, by means of these data Wynne-Jones²⁵ tested satisfactorily his linear relationship, $\log K_r \propto 1/D$ (where K_r is the ratio of the dissociation constant of a given acid to the dissociation constant of a reference acid, often the parent acid, and D is the dielectric constant of the solvent), deduced on the basis of electrostatic theory and involving simplifying assumptions such as neglect of non-electrostatic factors.²⁶ He suggested, for purposes of comparison, the use of "intrinsic strengths" derived by extrapolation to infinite dielectric constant; it is noteworthy, however, that these intrinsic strengths show the same sequence as the dissociation constants of the acids in water.³

A bibliography of measurements on acid strengths in non-aqueous solvents up to the year 1931 was provided by N. F. Hall;²⁷ a list of the references to later data for acids and bases in non-aqueous and partially aqueous solutions is included in the footnotes below.²⁸⁻⁴⁸ Almost always the temperature of experiment was 25°.

In a number of these investigations the Wynne-Jones relationship has been tested and found to be applicable^{37, 39, 42, 45, 46, 47, 49} (in the case of partially aqueous solutions the dielectric constant of the mixed solvent is varied by adjusting the proportions of the components). M. Kilpatrick

²⁴ *Chem. and Ind.*, 1933, **52**, 330.

²⁵ *Proc. Roy. Soc.*, 1933, **A**, **140**, 440; see also L. J. Minnick and M. Kilpatrick, *J. Physical Chem.*, 1939, **43**, 259.

²⁶ Compare *Ann. Reports*, 1934, **31**, 78. ²⁷ *Chem. Reviews*, 1931, **8**, 191.

²⁸ J. O. Halford, *J. Amer. Chem. Soc.*, 1931, **53**, 2944.

²⁹ M. Kilpatrick and M. L. Kilpatrick, *Chem. Reviews*, 1933, **13**, 131.

³⁰ V. K. LaMer and H. S. Downes, *J. Amer. Chem. Soc.*, 1933, **55**, 1840; *Chem. Reviews*, 1933, **13**, 47.

³¹ G. E. K. Branch, D. L. Yabroff, and collaborators, *J. Amer. Chem. Soc.*, 1933, **55**, 2935; 1934, **56**, 937, 1850, 1865.

³² J. W. Murray and N. E. Gordon, *ibid.*, 1935, **57**, 110.

³³ L. A. Wooten and L. P. Hammett, *ibid.*, p. 2289.

³⁴ G. M. Bennett, G. L. Brooks, and S. Glasstone, *J.*, 1935, 1821.

³⁵ S. Kilpi and H. Warsila, *Z. physikal. Chem.*, 1936, **A**, **177**, 427.

³⁶ F. H. Verhoek, *J. Amer. Chem. Soc.*, 1936, **58**, 2577.

³⁷ R. B. Mason and M. Kilpatrick, *ibid.*, 1937, **59**, 572.

³⁸ D. C. Griffiths, *J.*, 1938, 818.

³⁹ C. C. Lynch and V. K. LaMer, *J. Amer. Chem. Soc.*, 1938, **60**, 1252.

⁴⁰ W. C. Davies, *J.*, 1938, 1865.

⁴¹ H. H. Hodgson and R. Smith, *J.*, 1939, 263.

⁴² L. J. Minnick and M. Kilpatrick, *J. Physical Chem.*, 1939, **43**, 259.

⁴³ N. A. Izmailov, M. B. Schustova, and N. Vorodez, *J. Gen. Chem. Russia*, 1939, **9**, 598.

⁴⁴ J. N. Beliaev, *Kolloid Schurn.*, 1940, **6**, 531.

⁴⁵ B. Adell, *Z. physikal. Chem.*, 1940, **186**, 27.

⁴⁶ M. Kilpatrick and W. H. Mears, *J. Amer. Chem. Soc.*, 1940, **62**, 3047, 3051.

⁴⁷ J. H. Elliott and M. Kilpatrick, *J. Physical Chem.*, 1941, **45**, 454, 466, 472, 485.

⁴⁸ R. D. Kleene, F. H. Westheimer, and G. W. Wheland, *J. Amer. Chem. Soc.*, 1941, **63**, 791.

⁴⁹ H. S. Harned, *J. Physical Chem.*, 1939, **43**, 275.

and co-workers^{42, 47} and C. C. Lynch and V. K. LaMer³⁹ have demonstrated, nevertheless, that that the relationship does not hold when the medium possesses a dielectric constant of less than 20—25. J. H. Elliott and M. Kilpatrick⁴⁷ believe that this may be due to the larger part played by dipole interactions between acid and solvent, and E. C. Baughan⁵⁰ considers that such a breakdown might be expected. The first-mentioned authors also encountered lack of linearity with substituted benzoic acids in dioxan-water mixtures of D varying from 55 to 15, and they suggest that this possibly arises from a preferential orientation of dioxan molecules around the solute, which would cause a lower dielectric constant in the immediate vicinity of the acid molecules; L. A. Wooten and L. P. Hammett⁵³ also obtained little better than qualitative agreement. It is noteworthy that ordinarily the slopes of the straight lines obtained in the plot of $\log K$, against $1/D$ have a positive slope, *e.g.*, almost all *m*- and *p*-substituted benzoic acids, and are often roughly parallel; with *o*-substituted benzoic acids the lines are inclined in the opposite direction, although salicylic acid proves exceptional in this respect. Elliott and Kilpatrick attribute this feature to chelation between the substituent and the hydrogen of carboxyl in the case *o*-chloro- and *o*-nitro-benzoic acids, a view which conflicts with H. O. Jenkins's suggestion⁵¹ that the strengths of these acids (in water) can be adequately accounted for simply by ascribing to the groups their ordinary polar characteristics.

There can be no doubt that, despite the success which the Wynne-Jones relation has achieved, the chemical rôle of the solvent is by no means an insignificant factor governing the extent of acid dissociation. The intervention of this factor has been mentioned in earlier Reports and elsewhere.⁵² It is interesting to note that, although Minnick and Kilpatrick⁴² have stated that the relative strengths of carboxylic acids are the same in two solvents of identical dielectric constant, *viz.*, methyl and ethyl alcohols, on the one hand, and dioxan-water mixtures on the other, Elliott and Kilpatrick⁴⁷ now contradict this claim after further measurements with similar solvents but using a different method of procedure. Actually, it has been stressed more than once^{37, 53} that in order to test the Wynne-Jones expression satisfactorily, data referring to solvents of similar chemical type should be selected, and, moreover, the data should all be derived from a consistent experimental method.^{42, 47} It is possible that in these circumstances the chemical factor introduced by the solvent will be cancelled out. In support of this stipulation a few instances may be quoted in which a change in the chemical character of the solvent brings about a distinct increase in the strength of the dissolved acid, which cannot be attributed to the alteration

⁵⁰ *J. Chem. Physics*, 1939, 7, 951.

⁵¹ *J.*, 1939, 640.

⁵² L. P. Hammett, *J. Amer. Chem. Soc.*, 1928, 50, 2666; "Physical Organic Chemistry," New York, 1940, p. 256; *Ann. Reports*, 1930, 27, 326—356; J. O. Halford, *J. Amer. Chem. Soc.*, 1931, 53, 2939; C. A. Kraus, *J. Franklin Inst.*, 1933, 225, 702—707; J. F. J. Dippy, *Chem. Reviews*, 1939, 25, 166; *J.*, 1941, 550; W. F. Luder, *Chem. Reviews*, 1940, 27, 555—568.

⁵³ J. F. J. Dippy, *J.*, 1941, 550.

in the dielectric constant. Thus the acidity of hydrochloric acid in dioxan is increased by small additions of certain phenols and alcohols; ⁵⁴ this is thought to be due to hydrogen-bond formation between hydroxyl and chlorine. Again, the strengths of seven common monocarboxylic acids have been found to be slightly greater in 20% aqueous sucrose than in water, although the dielectric constant of the former solvent is appreciably smaller than that of the latter.⁵³ It is also noteworthy that acids of the ammonium-ion type (BH^+), the dissociation of which should be scarcely affected by a change of dielectric constant, show an increased acidity in ethyl alcohol as compared with water.⁵⁵ *

The various solvents employed so far include methyl, ethyl, and *n*-butyl alcohols, glycol, benzene, chlorobenzene, formamide and acetonitrile, and also aqueous methyl and ethyl alcohols, glycerol, dioxan, acetone and sucrose (the solvent in certain cases also contained some inert electrolyte, *e.g.*, lithium chloride). Among the acids and bases examined have been aliphatic acids, substituted benzoic, cinnamic and phenylboric acids, halogeno-phenols and -anilines, and substituted dimethylanilines. For the most part, potentiometric and colorimetric methods of measurement have been used.

In discussing the relative strengths of acids in a pair of solvents, J. O. Halford ^{56, 28} has pointed out that, although variations in relative strength with change of solvent are only minor among acids of one charge type, it might be unwise to draw conclusions, especially of a quantitative nature, where differences in absolute strength are less than $1p_K$ unit, *i.e.*, a factor of 10 in K .⁵⁷ Nevertheless, examination of the present evidence shows that the order of strengths is quite well preserved from solvent to solvent among uncharged acids differing in K by much less than this factor. A number of investigators have actually stated that their measurements on series of acids (and bases) in a given solvent reveal a close correspondence with the order of strengths in water. In some cases quantitative agreement has been noted; *e.g.*, N. F. Hall ⁵⁸ has shown that the relative strengths of a large number of organic bases in acetic acid and in water are nearly proportional. F. H. Verhock ³⁶ obtained straight lines on plotting p_K for solutions of a variety of carboxylic acids and phenols in formamide against values for aqueous solutions, and Wooten and Hammett ³³ arrived at a similar result with *m*- and *p*-substituted benzoic acids in *n*-butyl alcohol and water. Again, V. K. LaMer and H. C. Downes ³⁰ record that uncharged organic acids in benzene retain the same differences in strength among themselves that exist in water (salicylic acid is exceptional), thus going further

⁵⁴ P. D. Bartlett and H. J. Dauben, *J. Amer. Chem. Soc.*, 1940, **62**, 1339.

⁵⁵ See L. P. Hammett, "Physical Organic Chemistry," New York, 1940, p. 260.

⁵⁶ *J. Amer. Chem. Soc.*, 1931, **53**, 2939. ⁵⁷ Compare *Ann. Reports*, 1934, **31**, 78.

⁵⁸ *J. Amer. Chem. Soc.*, 1930, **52**, 5115.

* F. J. Moore and S. B. Johns (*J. Amer. Chem. Soc.*, 1941, **63**, 3336) have recently recorded that the ionisation constants of picric acid in acetone, methyl ethyl ketone, acetophenone, propionitrile, and benzonitrile depend less on the dielectric constant of the medium than on the electron-sharing ability of the radicals in the solvent molecule.

than J. N. Brönsted,⁵⁹ who showed good qualitative correspondence for benzene solutions; a similar conclusion was reached by D. G. Griffiths,³⁸ who used chlorobenzene as solvent. It is interesting that agreement is found with the measurements in aprotic solvents, *i.e.*, inert diluents having neither proton-accepting nor proton-donating character, in which it is to be expected that acids will exhibit their true relative strengths. This gives strong support for the practice of employing dissociation constants for aqueous solutions of acids in discussions concerning the polar influences of substituents. Indeed, the conclusion has been drawn^{3, 53} that existing data show that, *in general*, organic acids (uncharged) exhibit the same relative strengths in proceeding from solvent to solvent, provided that certain well-defined acids are excluded, particularly those in which there exists some specific interaction of groups. The qualification might be added that it is safer to restrict correlations to acids of similar class,⁶⁰ *i.e.*, where the reacting groups are alike. For instance, it is better to consider monocarboxylic acids as apart from phenols; thus Verhoek³⁶ found that the data for these two classes of acid gave separate straight lines in the plot of p_K for formamide and aqueous solutions. Notable anomalies are salicylic and *o*-toluic acids, where the hydroxyl and methyl substituents are believed to form a hydrogen-bond with the carboxyl group (on this basis *n*-butyric and higher aliphatic acids should also be anomalous). Wooten and Hammett³³ have made the important observation that, in transferring from water to *n*-butyl alcohol, any substituent which causes a rise in absolute strength causes an increase in relative strength (hence the positive slope in the plot of $\log K_r$ against $1/D$), the converse being true for a substituent which depresses absolute strength. They exclude from this generalisation not only *o*-substituted benzoic acids but α -substituted aliphatic acids as well (proximity effect). *o*-Substituted benzoic acids were among those acids which Burkhardt described as anomalous, and furthermore, they provide examples of negative slopes in the $\log K_r$ - $1/D$ plot. In such cases the abnormality caused by the operation of the additional factor might not be reproduced systematically in all solvents,³ because, as Hammett⁶¹ indicates, the chemical nature of the solvent can influence the extent of the abnormality. It is noteworthy, therefore, that whereas Elliott and Kilpatrick⁴⁷ have asserted that the relative strengths of *o*-, *m*- and *p*-nitro-, -halogeno-, -methyl-, -hydroxy- and -methoxy-benzoic acids in methyl, ethyl, and *n*-butyl alcohols and ethylene glycol do not present the same sequence as in water, a detailed examination of their results⁵³ reveals that, when the above anomalous acids are excluded, a very close correspondence with the data for aqueous solutions exists.

In conclusion, it may be said that, until an ideal method of comparing the strengths of weak acids is forthcoming, it would appear that the selection

⁵⁹ *Ber.*, 1928, **61**, 2049.

⁶⁰ See G. M. Bennett, G. L. Brooks, and S. Glasstone (ref. 34), and J. F. J. Dippy (ref. 3).

⁶¹ L. P. Hammett, "Physical Organic Chemistry," New York, 1940, p. 207.

of thermodynamic dissociation constants referring to the solvent water and a temperature of 25° is reasonable. The pronounced regularities disclosed by inspection of the existing data certainly seem to give it justification, and changes in the sequences of acid strengths occasioned by variations of temperature and solvent appear likely to be only of a minor character and to admit of a simple explanation consistent with the present views regarding the polar effects of substituents.

J. F. J. D.

3. ORGANOMETALLIC COMPOUNDS.

Since the appearance of the last reports ¹ on this subject, continued attention has been given to compounds of metals from all parts of the periodic table, largely in order to systematise on a broader basis their existence, composition, and reactions, and partly in view of their importance in medicine and the arts. Compounds of the less typically metallic elements have been excluded from the following account except for purposes of comparison.

General.^{2, 3}

The preparation of organic compounds of further elements or of new types is significant in view of attempts to define the kinds of derivatives possible to elements in the various regions of the periodic table. Triethylscandium and triethylyttrium ⁴ appear to be the first exceptions to A. von Grosse's generalisation ⁵ that the transition elements do not give compounds of the type R_nM , where n is the group valency of M towards hydrogen.

Among newer types may also be cited the reactive tri-alkyl or -aryl derivatives of gallium,^{6, 7, 8} indium,^{8, 9} and thallium,^{10, 11} together with the "mixed" gallium compounds Me_2GaCl and $MeGaCl_2$; ⁶ compounds of univalent thallium may also exist.¹¹ V. M. Pletz reports highly unstable butyltitanium ethoxides,¹² and there are indications of the formation of

¹ *Ann. Reports*, 1928, **25**, 92; 1932, **29**, 96, 98; see also 1937, **34**, 243.

² E. Krause and A. von Grosse, "Chemie der metall-organischen Verbindungen" (1937).

³ H. Gilman, "Organic Chemistry," Chap. 4 (1938).

⁴ V. M. Pletz, *Compt. rend. Acad. Sci. U.R.S.S.*, 1938, **20**, 27.

⁵ *Z. anorg. Chem.*, 1926, **152**, 145.

⁶ G. Renwanz, *Ber.*, 1932, **65**, 1308; C. A. Kraus and F. E. Toonder, *Proc. Nat. Acad. Sci.*, 1933, **19**, 292, 298; *J. Amer. Chem. Soc.*, 1933, **55**, 3547; L. M. Dennis and W. Patnode, *ibid.*, 1932, **54**, 182.

⁷ H. Gilman and R. G. Jones, *ibid.*, 1940, **62**, 980.

⁸ A. W. Laubengayer and W. F. Gilliam, *ibid.*, 1941, **63**, 477.

⁹ L. M. Dennis, R. W. Work, E. G. Rochow, and E. M. Chamot, *ibid.*, 1934, **56**, 1047; W. C. Schumb and H. I. Crane, *ibid.*, 1938, **60**, 306; H. Gilman and R. G. Jones, *ibid.*, 1940, **62**, 2353.

¹⁰ S. F. Birch, *J.*, 1934, 1132; E. G. Rochow and L. M. Dennis, *J. Amer. Chem. Soc.*, 1935, **57**, 486.

¹¹ H. Gilman and R. G. Jones, *ibid.*, 1939, **61**, 1513; 1940, **62**, 2357.

¹² *J. Gen. Chem. Russia*, 1938, **8**, 1298; cf. L. G. Makarova and A. N. Nesmejanov, *ibid.*, 1939, **9**, 771.

organo-vanadium¹³ and -tantalum compounds.¹⁴ Phenyl derivatives of molybdenum,¹⁵ tungsten,¹⁶ and manganese¹⁷ have been recorded, but full description is still lacking; tri(?)methylrhenum is described in a brief note.¹⁸ H. Gilman and M. Lichtenwaller¹⁹ have prepared the first "simple" organoplatinum compounds, Me_4Pt and Me_6Pt_2 .

TABLE I.

	M. p.	B. p.	Action of : air.	water.	cold HCl.
$\text{Et}_2\text{Sc}, \text{Et}_2\text{O}$	—	170—172°	++	+	
$\text{Et}_2\text{Y}, \text{Et}_2\text{O}$	—	222—225	+	+	
Me_3Ga	—19°	55.7	++	1CH_4	2CH_4
Me_3In	89	50/24 mm.	+	2CH_4	
Et_2Tl	—63	54.8/1.5 mm.	—	$1\text{C}_2\text{H}_4$	$1\text{C}_2\text{H}_4$
PhMnI	solid	—	++	+	
Me_3Re	—	ca. 60	—	—	—
Me_4Pt	cryst.	—			1CH_4

++ spontaneously inflammable.

Physicochemical Properties.—The vapour density⁸ of trimethylaluminium at 70° corresponds to the formula Al_2Me_6 , and the values at higher temperatures indicate a heat of dissociation of some 20 cal., comparable with that of the dimeric aluminium halides. The usual formulation (I) for the latter is not applicable to the alkyls, and the possibility of Al—Al bonding is considered²⁰ to be supported by determinations of the dipole moments of trimethylaluminium and the methylaluminium halides. Triethylaluminium also is associated in the vapour state, but triethylgallium and trimethylindium are not.⁸ An elaborate study²¹ has been made of the molecular volumes, heats of combustion, and refractivities of numerous alkyl derivatives of mercury, tin, lead, and the group V metals. A. von Grosse^{2,5} discusses the physical constants of organic compounds of the elements in relation to the periodic table.

Electrolysis of a series of alkylmagnesium halides in ethyl or butyl ether²² gave one equivalent of magnesium per Faraday at the cathode, and one molecule of magnesium halide at the anode. With methylmagnesium halides ethane is the predominant gaseous product at high current densities;

¹³ C. C. Vernon, *J. Amer. Chem. Soc.*, 1931, **53**, 3831; A. V. Kirsanov and T. V. Sazonova, *J. Gen. Chem. Russia*, 1935, **5**, 956.

¹⁴ B. N. Afanasyev, *Chem. and Ind.*, 1940, **59**, 631.

¹⁵ F. Hein, *Angew. Chem.*, 1938, **51**, 503.

¹⁶ F. Hein and E. Nebe, *Naturwiss.*, 1940, **28**, 93.

¹⁷ H. Gilman and J. C. Bailie, *J. Org. Chem.*, 1937, **2**, 84.

¹⁸ J. G. F. Druce, *J.*, 1934, 1129; cf. H. Gilman, R. G. Jones, F. W. Moore, and M. J. Kolbezen, *J. Amer. Chem. Soc.*, 1941, **63**, 2525.

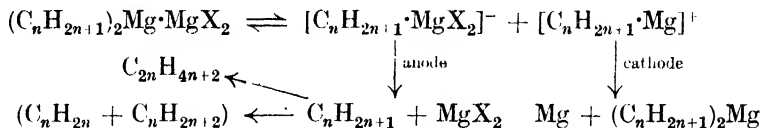
¹⁹ *Ibid.*, 1938, **60**, 3085.

²⁰ R. H. Wiswall and C. P. Smyth, *J. Chem. Physics*, 1941, **9**, 352; cf. L. O. Brockway and N. R. Davidson, *J. Amer. Chem. Soc.*, 1941, **63**, 3287.

²¹ W. J. Jones *et al.*, *J.*, 1931, 2109; 1932, 2284; 1935, 39; *Bull. Soc. chim.*, 1931, **49**, 187; *J. Physical Chem.*, 1933, **37**, 583.

²² W. V. Evans *et al.*, *J. Amer. Chem. Soc.*, 1934, **56**, 654; 1935, **57**, 489; 1936, **58**, 720, 2284; 1939, **61**, 898; 1940, **62**, 534; 1941, **63**, 2574.

its nearly complete supersession by methane (derived from reaction with the solvent) at low c. d.'s suggests that the methyls are not liberated in pairs. The higher alkylmagnesium compounds give the corresponding alkane and alkylene with quantities of dialkyl increasing from traces with the ethyl and *isopropyl* through *tert.*-butyl and *n*-propyl to nearly exclusive production of octanes from the other butyl derivatives and of dodecane from the *n*-hexyl. The main reactions are formulated :



Arylmagnesium halides give much polyaryl, some diaryl, and much styrene from interaction with the solvent.

Conductivity measurements and general considerations led K. A. Jensen²³ to attribute covalent structures to mixed organometallic compounds, their conductivity in water and in many cases their solubility depending on the formation of aquo-complexes— $\text{R}_3\text{SnX} + \text{H}_2\text{O} \rightleftharpoons [\text{R}_3\text{Sn} \cdot \text{OH}_2]\text{X}$. C. P. Smyth,²⁴ from studies of the dipole moments, concludes that many metal-halogen bonds are largely ionic, although the carbon-metal linkages are covalent.

The compounds formulated as Ph_5CrX , Ph_4CrX , and Ph_3CrX have magnetic moments approximating to 1.73 Bohr magnetons and are believed to contain quinquevalent chromium. It is suggested²⁵ that these substances, some of which yield much diphenyl on decomposition, may really contain diphenyl groups and be $[\text{C}_6\text{H}_4\text{Ph} \cdot \text{CrPh}_3]\text{X}$, $[\text{C}_6\text{H}_4\text{Ph} \cdot \text{CrPh}_2\text{H}]\text{X}$, and $[\text{C}_6\text{H}_4\text{Ph} \cdot \text{CrPhH}_2]\text{X}$.

Mercury-olefin Complexes.—Mercuric salts in water or alcohol combine with ethylene, yielding products which are usually formulated as $\text{RO} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{HgX}$ (Ia) and $\text{O}[\text{CH}_2 \cdot \text{CH}_2 \cdot \text{HgX}]_2$; owing to the ready regeneration of ethylene they have also been regarded as Werner complexes:²⁶ $[\text{RO} \cdot \text{Hg} \cdot \text{C}_2\text{H}_4]\text{X}$ (Ib) and $[\text{C}_2\text{H}_4 \cdot \text{Hg} \cdot \text{O} \cdot \text{Hg} \cdot \text{C}_2\text{H}_4]\text{X}_2$. After it had been discovered²⁷ that diaryltin dichlorides react with inorganic mercury compounds to give diarylmercury but with alkylmercury halides furnish mixed alkylarylmercury, the reaction was applied²⁶ to the compound (I; $\text{R} = \text{H}$, $\text{X} = \text{Br}$). This gave only hydroxyethyl-*p*-tolylmercury (which afforded ethylene quantitatively with hydrochloric acid!). On the other hand,

²³ *Z. anorg. Chem.*, 1937, **230**, 277.

²⁴ *J. Org. Chem.*, 1941, **6**, 421; G. L. Lewis, P. F. Oesper, and C. P. Smyth, *J. Amer. Chem. Soc.*, 1940, **62**, 3243.

²⁵ *Amer. Chem. Soc.*, 1940, **62**, 3243.

²⁶ Summary: A. N. Nesmejanov and R. C. Freidlina, *Compt. rend. Acad. Sci. U.R.S.S.*, 1940, **26**, 60; *Ber.*, 1936, **69**, 1631; R. N. Keller, *Chem. Reviews*, 1941, **28**, 229.

²⁷ A. N. Nesmejanov and K. A. Kotscheschkov, *Ber.*, 1934, **67**, 317; *idem* and R. C. Freidlina, *Ber.*, 1935, **68**, 565.

the substances $\text{HgCl}_2 \cdot \text{C}_2\text{H}_2$ and $\text{HgCl}_2 \cdot 2\text{C}_2\text{H}_2$ yielded diarylmercury, and triphenylphosphine displaced acetylene from them, giving $\text{HgCl}_2 \cdot \text{PPh}_3$.²⁶ In an attempted rational synthesis of (Ia, $\text{R} = \text{Et}$),²⁸ the salt $\text{EtO} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{SO}_2 \cdot \text{HgCl}$ was boiled with water, but ethylene was produced quantitatively. Since ethylene is formed from $\text{EtO} \cdot \text{CH}_2 \cdot \text{CH}_2\text{Br}$ and Mg ,²⁹ and from $\text{CPh}_3 \cdot \text{CH}_2 \cdot \text{CH}_2\text{I}$ and Na ,³⁰ and the volatile and no doubt correctly formulated "Lewistite," $\text{CHCl} \cdot \text{CH} \cdot \text{AsCl}_2$, affords acetylene on treatment with alkali, it seems dangerous to base co-ordination formulæ on the mere ready regeneration of unsaturated hydrocarbon. R. C. Freidlina and A. N. Nesmejanov²⁶ emphasise the continuity in behaviour from admitted principal valency compounds through substances of controversial structure to recognised Werner complexes, and offer spectroscopic evidence that resonance between the two types occurs in mercuric chloride-acetylene compounds. H. J. Lucas and S. Winstein have expressed similar views.³¹

General Chemical Behaviour.—With compounds containing active hydrogen, organometallic substances undergo fission, $\text{RM} + \text{HX} \longrightarrow \text{RH} + \text{MX}$, which proceeds with very different degrees of facility, the more easily, broadly speaking, the baser the metal (compare Tables I and II). Free hydrogen at room temperature decomposes reactive organometallic compounds analogously,³² $\text{PhNa} + \text{H}_2 \longrightarrow \text{PhH} + \text{NaH}$, the speed increasing in the order PhCaI , PhLi , PhNa , PhK , PhRb , PhCs . The reaction may be influenced by other, more specific, properties of the reagent as well as by its acidity. Thus tetraethyl-lead and triethyl-bismuth are unaffected by organic acids under mild conditions, but yield ethane quantitatively with thiols, and have been recommended for the "Zerevitinov" determination of SH in presence of OH or NH.³³

Different organic radicals, moreover, are not detached equally readily. The partial scission of unsymmetrical mercury compounds enables radicals to be arranged in a series^{1, 34} of decreasing lability which is regarded as a series of diminishing electronegativity: α -thienyl $>$ *o*- and *p*-anisyl $>$ α -naphthyl $>$ *o*-, *m*-, and *p*-tolyl $>$ phenyl and halogenophenyl $>$ *n*- and many other alkyls $>$ benzyl $>$ *tert*-butyl and *neopentyl*. Compounds of other metals furnish series very similar but less elaborately investigated—*germanium*:³⁵ *p*-tolyl $>$ *m*-tolyl $>$ phenyl $>$ benzyl; *tin*:³⁶ α -thienyl $>$

²⁸ J. D. Loudon and N. Shulman, *J.*, 1939, 1066.

²⁹ R. C. Tallman, *J. Amer. Chem. Soc.*, 1934, **56**, 126.

³⁰ C. B. Wooster and R. A. Morse, *ibid.*, p. 1735.

³¹ *ibid.*, 1938, **60**, 836; 1939, **61**, 3102 (with F. R. Hepner).

³² H. Gilman, A. L. Jacoby, and (Miss) H. Ludeman, *J. Amer. Chem. Soc.*, 1938, **60**, 2336; see also W. H. Zartman and H. Adkins, *ibid.*, 1932, **54**, 3398.

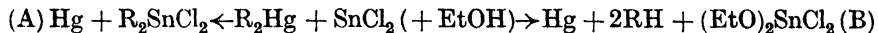
³³ H. Gilman and J. F. Nelson, *ibid.*, 1937, **59**, 935.

³⁴ M. S. Kharasch, H. Pines, and (Miss) J. H. Levine, *J. Org. Chem.*, 1938, **3**, 347; M. S. Kharasch and S. Swartz, *ibid.*, p. 405; M. S. Kharasch, R. R. Legault, and W. R. Sprouls, *ibid.*, p. 409; F. C. Whitmore and H. Bernstein, *J. Amer. Chem. Soc.*, 1938, **60**, 2626.

³⁵ J. K. Simons, *ibid.*, 1935, **57**, 1299.

³⁶ T. S. Bobaschinskaja and K. A. Kotscheschkov, *J. Gen. Chem. Russia*, 1938, **8**, 1850.

p-anisyl > α -naphthyl > phenyl > cyclohexyl; lead: ³⁷ α -furyl > α -thienyl, *p*-anisyl > phenyl > ethyl, benzyl; α -naphthyl > phenyl. A. N. Nesmejanov and K. A. Kotscheschkov ³⁸ describe a transformation in which elimination of a radical as hydrocarbon is in competition with an alternative mode of reaction:



Dominance of the mode (A) is associated with "electronegativity" of R, and decreases in the order: *p*-C₆H₄·NH₂, *p*-C₆H₄·OH, *o*-anisyl, β -naphthyl, *o*- and *p*-tolyl, *p*-halogenophenyl, phenyl, *p*-C₆H₄·CO₂Et, benzyl, ethyl.

Much elaborate work has been done on the relation between the reactivity of an organometallic compound and the nature of the metal, especially its position in the periodic table. Mutually compatible results are obtained only with important restrictions as to the reactions employed in assessing reactivities. Thus ease of thermal decomposition and of atmospheric oxidation show little connection with one another or with sensitiveness to water and acids, but the last property runs roughly parallel with the synthetically important power of addition to multiple linkages. Table II shows the behaviour of derivatives of a number of metals towards different reagents; more precise comparisons, often with benzonitrile as substrate, have led H. Gilman to the following inequalities in "reactivity": RCs > RRb > RK > RNa \gg RLi > RMgBr (R = CPh:C·); ³⁹ RLi > RMgX or R₂Mg; ⁴⁰ PhLi > PhCaI > PhMgI; ⁴¹ RMgX > R₃Al > R₃B > R₂Zn; ⁴² R₂Zn > R₂Cd > R₂Hg; ⁴³ R₃Al \gg R₃Tl; Ph₃In > Ph₃Ga \gg Ph₃Tl. ^{7,9}

TABLE II.

	CH ₂ :CPh ₂	R ₂ CO.	R·COCl.	NH ₃ .	H ₂ O.	HCl, aq.		R ₂ CO.	R·COCl.	NH ₃ .	H ₂ O.	HCl, aq.
RNa	++	++	++	++	++	++	RCu ⁴⁶	++	++		++	++
RLi	++	++	++	++	++	++	RAg ⁴⁶	+	++			
RBaX		++			++	++	R ₂ Zn ⁴²	+	++	++	++	++
RCaX ⁴⁴	?	++	-?		++	++	R ₂ Cd ^{43, 47}	+	++	+	++	++
RMgX	- ⁴⁵	++	++	++	++	++	R ₂ Hg	-	+	+	++	++
R ₄ Be	-	++	++		++	++	R ₄ Pb	-	+	-	++	++
R ₂ B		+		-	-	+	R ₄ Sn	-	+		+	+
R ₂ Al ⁴²		+	++	++	++	++	R ₃ Bi	-	+	-	++	++
R ₃ Ga ^{6, 7}		+	+	-	++	++	R ₃ Sb	-		-	+	+
R ₃ In ⁹		+		-	++	++						
R ₃ Tl ¹¹		+	++		++	++						

Rapid action at or near room temp. is indicated by ++, no action under ordinary conditions by -; mere addition of NH₃ is disregarded. See also ref. 3.

³⁷ H. Gilman and E. B. Towne, *Rec. Trav. chim.*, 1932, **51**, 1054; *J. Amer. Chem. Soc.*, 1933, **55**, 4689 (with H. L. Jones); 1939, **61**, 739.

³⁸ *Ber.*, 1930, **63**, 2496; *Sci. Rep. Moscow State Univ.*, 1934, No. 3, 283.

³⁹ H. Gilman and R. V. Young, *J. Org. Chem.*, 1936, **1**, 315.

⁴⁰ H. Gilman and R. H. Kirby, *J. Amer. Chem. Soc.*, 1933, **55**, 1265; H. Gilman and M. Lichtenwalter *Rec. Trav. chim.*, 1936, **55**, 561.

⁴¹ H. Gilman, R. H. Kirby, M. Lichtenwalter, and R. V. Young, *ibid.*, p. 79.

⁴² H. Gilman and K. E. Marple, *ibid.*, p. 133.

⁴³ H. Gilman and J. F. Nelson, *ibid.*, p. 518.

H. Gilman associates the alternative courses of some reactions with the reactivity of the organometallic participant. Derivatives of the alkali metals and calcium undergo predominantly normal addition to the carbonyl group of benzylideneacetone and the like, whereas many others afford finally the saturated ketone $\text{CHPhR} \cdot \text{CH}_2 \cdot \text{COMe}$ —"1:4-addition".⁴⁹ The former reagents similarly convert benzophenoneanil normally into triphenylmethylaniline,⁴⁹ and phenylmagnesium bromide attacks the nucleus, giving *o*-phenylbenzhydrylaniline, $\text{C}_6\text{H}_4\text{Ph} \cdot \text{CHPh} \cdot \text{NHPH}$. With azobenzene,¹⁷ aryl compounds of potassium and calcium afford triphenylhydrazine, whereas those of other metals, including sodium and lithium, yield hydrazobenzene and/or aniline by reduction.

H. Gilman and J. F. Nelson^{3, 43} relate the reactivity of organometallic compounds to the position of the metal in the periodic table by a series of rules which somewhat outrun the experimental data. Broadly speaking, in each group, $\text{Li}-\text{Cs}$, $\text{Be}-\text{Ca}$, $\text{B}-\text{Al}$, $\text{C}-\text{Pb}$, and $\text{N}-\text{Bi}$, the reactivity of the organic derivatives rises with the atomic weight of the metal, and falls with increasing group number from I to IV. In each B group, $\text{Cu}-\text{Ag}$, $\text{Zn}-\text{Hg}$, and $\text{Ga}-\text{Tl}$, the reactivity is less than in the corresponding A group and appears to fall with increasing atomic weight of the metal. In many cases the mixed organic compounds of a metal are a little less reactive than the simple ones, but substances of the types RBX_2 and R_2TX are extraordinarily inert in comparison with R_3B or R_3Ti .

Attempts to correlate by various methods the reactivity of Grignard reagents with the nature of the hydrocarbon radical have given contradictory results.⁵⁰

A redistribution of organic radicals between metallic atoms, as in the case $\text{Me}_2\text{Hg} + \text{Et}_2\text{Hg} \rightleftharpoons 2\text{MeEtHg}$, has been occasionally encountered, and now forms the subject of an elaborate study by G. Calingaert and co-workers.⁵¹ In the example cited, the equilibrium mixture attained from either direction contains 50 molecules % of the mixed dialkylmercury and 25% of each of the simple ones, corresponding to a random distribution of radicals between the metallic atoms. If excess of one dialkylmercury is taken, the new equilibrium corresponds to a new random distribution, and the same holds for the more complicated case of a pair of alkyl-leads which gives a mixture of R_4Pb , $\text{R}_3\text{R}'\text{Pb}$, $\text{R}_2\text{R}'_2\text{Pb}$, $\text{RR}'_3\text{Pb}$, and $\text{R}'_4\text{Pb}$.

⁴⁴ C. Glacet, *Bull. Soc. chim.*, 1938, **5**, 895.

⁴⁵ C. R. Kinney and R. G. Larsen, *J. Amer. Chem. Soc.*, 1935, **57**, 1054.

⁴⁶ H. Gilman and J. M. Straley, *Rec. Trav. chim.*, 1936, **55**, 821.

⁴⁷ A. N. Nesmejanov and L. G. Makarova, *J. Gen. Chem. Russia*, 1937, **7**, 2649.

⁴⁸ N. N. Melnikov and M. S. Rokitskaja, *ibid.*, p. 464; H. Gilman and J. F. Nelson, *J. Amer. Chem. Soc.*, 1939, **61**, 743.

⁴⁹ H. Gilman and R. H. Kirby, *ibid.*, 1941, **63**, 2046.

⁵⁰ H. Gilman, (Miss) E. L. St. John, (Miss) N. B. St. John, and M. Lichtenwalter, *Rec. Trav. chim.*, 1936, **55**, 577 (literature); M. S. Kharasch and S. Weinhouse, *J. Org. Chem.*, 1936, **1**, 209.

⁵¹ *J. Amer. Chem. Soc.*, 1939, **61**, 2748, 2755, 2758, 3300; 1940, **62**, 1099, 1104, 1107, 1542; 1941, **63**, 947.

With derivatives of mercury, lead, tin, and silicon, these equilibria are rapidly established, usually in boiling hexane in presence of metallic or alkylmetallic chlorides, conveniently aluminium chloride. The stability in the absence of a catalyst of pure MeEtHg and the like is emphasised.⁵²

Radioactive "labelling" discloses the interaction of tetraethyl-lead and triethyl-lead chloride, $\text{Et}_4\text{Pb}^* + \text{Et}_3\text{PbCl} \longrightarrow \text{Et}_4\text{Pb} + \text{Et}_3\text{Pb}^*\text{Cl}$, and the equilibration was studied of mixtures such as $\text{Me}_4\text{Pb}-\text{Et}_3\text{PbCl}$ which gave five tetra-alkyl-leads and four trialkyl-lead chlorides. All these equilibria are independent of solvent, catalyst, and temperature. Since the reactions proceed quantitatively without formation of by-products, and especially because *n*-propyl groups suffer no isomerisation to isopropyl, it is considered improbable that free alkyl radicals or ions play a part.

Equilibration of $(2\text{Me}_2\text{Hg} + \text{Et}_4\text{Pb})$ or of $(2\text{Et}_2\text{Hg} + \text{Me}_4\text{Pb})$ led to the same mixture, such that in the alkyl-lead compounds considered as a group there was random distribution of methyl and ethyl radicals, and similarly in the mercurials. But over all some $\frac{2}{3}$ of the methyls were combined with mercury and $\frac{1}{3}$ with lead—"mercury shows a greater affinity than lead for methyl with respect to ethyl radicals."

Radical exchanges have also been observed between compounds of lithium and magnesium on the one hand, and those of mercury, lead, and bismuth on the other.⁵³ In some cases reversibility has been established, and the influence of the nature of the metals and radicals on the ease of reaction has been examined. The disproportionation, $4\text{R}_3\text{Pb} \longrightarrow 3\text{R}_4\text{Pb} + \text{Pb}$, has also been studied.⁵⁴

Aryltin halides are advantageously prepared by heating a tetra-aryltin or an aryltin halide with a less highly arylated tin halide or a stannic halide in appropriate proportions. The method is applicable to the alkyl series with the limitation that alkyltin trihalide is never produced.⁵⁵ A. von Grosse and J. M. Mavity⁵⁶ have studied the complete series of analogous (reversible) changes involving alkylaluminium halides and in some cases ethoxides; and similar transformations of thallium compounds are recorded.⁵⁷ Di-*n*-butyl-lead dichloride decomposes at 130° : $2\text{Bu}_2\text{PbCl}_2 \longrightarrow \text{BuCl} + \text{PbCl}_2 + \text{Bu}_3\text{PbCl}$.⁵⁸

The mixed organometallic compounds can often be converted into the corresponding simple ones by the action of reducing agents. Hydrazine is strongly recommended for the transformation of RHgX into R_2Hg , and

⁵² Cf., e.g., M. S. Kharasch and R. Marker, *J. Amer. Chem. Soc.*, 1926, **48**, 3130.

⁵³ H. Gilman, H. L. Yablunsky, and A. C. Svigoon, *J. Amer. Chem. Soc.*, 1939, **61**, 1170; H. Gilman and F. W. Moore, *ibid.*, 1940, **62**, 3206; H. Gilman and R. G. Jones, *ibid.*, 1941, **63**, 1439, 2482 (with F. W. Moore).

⁵⁴ H. Gilman and J. C. Bailie, *ibid.*, 1939, **61**, 731.

⁵⁵ K. A. Kotscheschkov, *Ber.*, 1933, **66**, 1861; K. A. Kotscheschkov, M. M. Nadj, and A. P. Alexandrov, *Ber.*, 1934, **67**, 1348.

⁵⁶ *J. Org. Chem.*, 1940, **5**, 106.

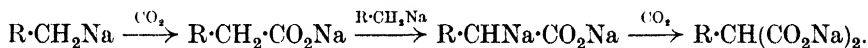
⁵⁷ N. N. Melnikov and G. P. Gratscheva, *J. Gen. Chem. Russia*, 1935, **5**, 1786.

⁵⁸ D. P. Evans, *J.*, 1938, 1466.

works well with lead and bismuth but not with tin compounds.⁵⁹ Metallic sodium is serviceable with alkylaluminium halides,⁵⁶ and tin or sodium-tin alloy with aryltin halides;⁶⁰ in each case the reaction may be conducted stepwise. The Grignard reagent ($2\text{RMgX} \rightleftharpoons \text{R}_2\text{Mg} + \text{MgX}_2$) affords solutions of R_2Mg by precipitation of the other components with dioxan, but the validity of the method for determining the position of equilibrium is disputed.⁶¹

*Preparative Methods.**

A. A. Morton and co-workers have made further studies of the preparation of organosodium derivatives by the classical method of interaction of metal and halide.^{62, 63} The reaction appears to be complicated by the formation of alkylene- or arylene-disodium, possibly from disproportionation of the primary product, as indicated by the appearance of dibasic acids on treatment with carbon dioxide. Control experiments suggest that these are not produced by the stages



It is, however, admitted that these changes are profoundly influenced by the physical condition of the reactants, and H. Gilman and H. A. Pacevitz have shown that formation of malonic acids is largely suppressed by the use of *solid* carbon dioxide.⁶⁴

The same preparative method has been applied to calcium⁴⁴ and thoroughly studied in the case of aluminium.^{56, 65} Here the lower alkyl and some aryl halides, without a solvent but in presence of iodine or aluminium chloride, gave a mixture of R_2AlX and RAlX_2 . By using magnalium the former compound was obtained exclusively.

The device of alkylating a compound of a metal in a lower valency state has been applied to plumbites, $\text{RI} + \text{Na}_2\text{PbO}_2 \longrightarrow \text{R}\cdot\text{PbO}_2\text{Na} + \text{NaI}$, yielding feebly amphoteric plumbonic acids convertible into the halides RPbX_3 ; ⁶⁶ and complex caesium chlorides afford derivatives of germanium,⁶⁷ tin,⁶⁸ and lead: ⁶⁹ $\text{RI} + \text{Cs}[\text{MX}_3] \longrightarrow \text{RMX}_3 + \text{CsI}$. Tetraphenyl-stibonium, -arsonium, and -phosphonium salts are obtained by the combination of the triaryl compound with aryl halide in presence of aluminium chloride.⁷⁰

Diazonium salts afford organometallic derivatives with the free heavy

⁵⁹ H. Gilman and M. M. Barnett, *Rec. Trav. chim.*, 1936, **55**, 563; H. Gilman and H. L. Yablunsky, *J. Amer. Chem. Soc.*, 1940, **62**, 665.

⁶⁰ M. M. Nadj and K. A. Kotscheschkov, *J. Gen. Chem. Russia*, 1938, **8**, 42.

⁶¹ A. C. Cope, *J. Amer. Chem. Soc.*, 1935, **57**, 2238; 1938, **60**, 2215; C. R. Noller and W. R. White, *ibid.*, 1937, **59**, 1354.

⁶² *Ibid.*, 1936, **58**, 1697; 1938, **60**, 1426, 1924; 1940, **62**, 120, 123, 126, 129.

⁶³ *Ibid.*, 1936, **58**, 2599; 1941, **63**, 324, 327.

⁶⁴ *Ibid.*, 1940, **62**, 1301.

⁶⁵ V. F. Hnizda and C. A. Kraus, *ibid.*, 1938, **60**, 2276.

⁶⁶ M. Lesbre, *Compt. rend.*, 1935, **200**, 559; 1940, **210**, 535.

⁶⁷ A. Tchakirian and M. Lewinsohn, *ibid.*, 1935, **201**, 835.

⁶⁸ *Idem* and M. Lesbre, *ibid.*, 1936, **202**, 138.

⁶⁹ M. Lesbre, *ibid.*, 1937, **204**, 1822.

⁷⁰ J. Chatt and F. G. Mann, *J.*, 1940, 1192.

* See also last two paragraphs.

metals,⁷¹ with compounds of the metal in a lower state of valency, as in the Bart reaction,⁷² $\text{RN}_2\cdot\text{X} + \text{Na}\cdot\text{AsO}_3\text{H}_2 \longrightarrow \text{R}\cdot\text{AsO}_3\text{H}_2$, or with the metallic halide, usually in presence of copper. The last method gives moderate to good yields of diarylmercury or arylmercury chloride,⁷³ diaryltin dichloride,⁷⁴ and triarylismuth,⁷⁵ and small quantities of triaryl-lead chloride.⁷⁴ Without copper, benzenediazonium chloride and phenylantimony dichloride give diphenylantimony trichloride.⁷⁶ These methods offer a route to compounds having reactive substituents which would forbid the use of, say, the Grignard reagent. Diazo-compounds may also be involved in the formation of organometallic compounds from phenylhydrazine and such oxidising agents as mercuric acetate or arsenic acid.⁷⁷

Mercuration, the most familiar case of the production of an organo-metallic compound from a hydrocarbon and a metallic salt, takes place in the β -position in pyridine,⁷⁸ and much more easily in the α -positions of furans⁷⁹ and γ -pyrones,⁸⁰ often with expulsion of carboxyl. A "plumbation" with loss of carbon dioxide occurs in an ingenious synthesis⁸¹ of carboxymethyltriphenyl-lead: $\text{CO}_2\text{Et}\cdot\text{CH}_2\cdot\text{CO}_2\text{Na} + \text{Ph}_3\text{PbCl} \longrightarrow \text{CO}_2\text{Et}\cdot\text{CH}_2\cdot\text{CO}_2\cdot\text{PbPh}_3 \xrightarrow{160^\circ} \text{CO}_2\text{Et}\cdot\text{CH}_2\cdot\text{PbPh}_3$. Auric chloride reacts energetically with aromatic hydrocarbons, giving rather unstable arylgold dichlorides.⁸²

Mercuric chloride displaces the acid substituent from aryl-boric or -sulphinic acids. The method has been extended to the preparation from camphor-10-sulphinic acid of the mercurichloride and, using arsenic trichloride, of the dichloroarsine;⁸³ and arylthallium compounds with reactive substituents have been obtained from arylboric acids and thallic bromide.⁸⁴ The iodoxy-group is displaced similarly by mercuric oxide: $\text{ArIO}_2 + \text{HgO} \longrightarrow \text{ArHg}\cdot\text{IO}_3$.⁸⁵

⁷¹ *Ann. Reports*, 1940, **37**, 278.

⁷² Modified by G. O. Doak, *J. Amer. Chem. Soc.*, 1940, **62**, 167.

⁷³ A. N. Nesmejanov, N. T. Gluschnov, P. T. Epifanski, and A. I. Flegontov, *Ber.*, 1934, **67**, 130; M. F. W. Dunker, E. B. Starkey, and G. L. Jenkins, *J. Amer. Chem. Soc.*, 1936, **58**, 2308.

⁷⁴ K. A. Kotscheschkov, A. N. Nesmejanov, and V. A. Klimova, *Ber.*, 1935, **68**, 1877.

⁷⁵ H. Gilman and A. C. Svigoon, *J. Amer. Chem. Soc.*, 1939, **61**, 3586; H. Gilman and H. L. Yablunky, *ibid.*, 1941, **63**, 949.

⁷⁶ A. B. Bruker, *J. Gen. Chem. Russia*, 1936, **6**, 1823.

⁷⁷ O. A. Seide, S. M. Scherlin, and G. J. Bras, *J. pr. Chem.*, 1933, **138**, 55, 225.

⁷⁸ W. M. Swaney, M. J. Skeeters, and R. N. Shreve, *Ind. Eng. Chem.*, 1940, **32**, 360.

⁷⁹ H. Gilman and G. F. Wright, *J. Amer. Chem. Soc.*, 1933, **55**, 3302.

⁸⁰ J. R. Files and F. Challenger, *J.*, 1940, 663.

⁸¹ K. A. Kotscheschkov and A. P. Alexandrov, *Ber.*, 1934, **67**, 527.

⁸² M. S. Kharasch and H. S. Isbell, *J. Amer. Chem. Soc.*, 1931, **53**, 3053

⁸³ J. D. Loudon, *J.*, 1933, 823; 1937, 391.

⁸⁴ N. N. Melnikov and M. S. Rokitskaja, *J. Gen. Chem. Russia*, 1937, **7**, 1472; cf. F. Challenger and (Miss) B. Parker, *J.*, 1931, 1462.

⁸⁵ A. N. Nesmejanov and L. G. Makarova, *Ber.*, 1933, **66**, 199.

Double decomposition between a metallic halide and an organic compound of another metal usually results in the transference of the organic radical to the nobler metal, so contrasting with and usefully supplementing the displacement of one metal by another. The Grignard reagent has thus furnished triethylscandium and triethylyttrium,⁴ trimethylrhenum,¹⁸ and aryltungsten derivatives from $W(OPh)_6$; ¹⁶ further study has been made of the preparation of copper, silver,⁴⁶ cadmium,⁴³ gallium,⁶ and unsymmetrical bismuth compounds.⁸⁶ An organolithium compound is necessary for the replacement of the third halogen atom of a thallic halide.^{10, 11} Cadmium bromide yields with phenyl-lithium diphenylcadmium, which in turn arylates mercuric, stannic, and antimonous chlorides.⁴⁷ Ether-free trimethylgallium has been obtained by using dimethylzinc.⁶

As would be expected, mercuric chloride exchanges chlorine for radicals attached to most metals. Compounds of tin, lead, and tervalent antimony are progressively dearylated; ²⁷ those of arsenic and quinquevalent antimony, but not quinquevalent bismuth,⁸⁷ are resistant. Mercuric oxide yields diarylmercury with derivatives of tin, lead, and tervalent antimony, arsenic,^{27, 88} and boron.^{27, 89} Mixed mercurials $RR'Hg$ are advantageously prepared from alkyl- or aryl-mercury hydroxides and diaryltin oxides.²⁷ These reactions sometimes proceed in the opposite sense, *e.g.*, $Ar_2Hg + TlBr_3 \longrightarrow Ar_2TlBr + HgBr_2$; ⁸⁴ it is more surprising that organolead compounds react with aluminium chloride.⁹⁰

The old and valuable method in which another metal displaces mercury from its organic derivatives has been applied to gallium ⁷ and indium.⁹ Such reactions often proceed in the sense that the baser metal replaces the nobler, but they are often reversible and there are many anomalies.⁹¹

The "*metalation*" ^{63, 92} of hydrocarbons or their derivatives, $RH + R'M \longrightarrow RM + R'H$, is usually limited to cases in which M is K, Na, Li, or Ca; it is favoured by the acidity of RH and also influenced by the nature of R'. Butyl-lithium, for example, will metalate diarylmethanes, and less easily toluene, naphthalene, or diphenyl; benzene reacts in the cold with ethylsodium or ethylpotassium but not with ethyl-lithium. Tolylsodium rearranges to benzylsodium on warming, but tolyl-lithium does not. 9:10-Dihydroanthracene is metalated in the *meso*-positions by butyl-lithium, and a similar reaction takes place with 1:4-dihydro-naphthalene,

⁸⁶ H. Gilman and H. L. Yablunky, *J. Amer. Chem. Soc.*, 1941, **63**, 207.

⁸⁷ L. G. Makarova, *J. Gen. Chem. Russia*, 1937, **7**, 143.

⁸⁸ K. A. Kotscheschkov and M. M. Nadj, *Ber.*, 1934, **67**, 717.

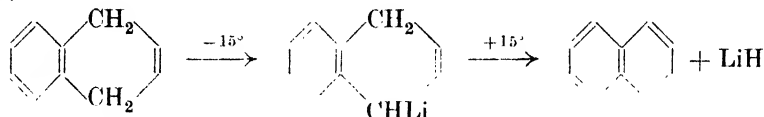
⁸⁹ F. Challenger and O. V. Richards, *J.*, 1934, 405.

⁹⁰ H. Gilman and L. D. Apperson, *J. Org. Chem.*, 1939, **4**, 162.

⁹¹ T. V. Talalaeva and K. A. Kotscheschkov, *J. Gen. Chem. Russia*, 1938, **8**, 1831.

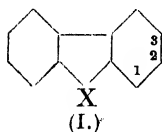
⁹² H. Gilman *et al.*, *J. Org. Chem.*, 1936, **1**, 146; 1938, **3**, 108, 120; *J. Amer. Chem. Soc.*, 1934, **56**, 1123, 1415; 1935, **57**, 1121; 1936, **58**, 2074; 1938, **60**, 2333; 1939, **61**, 106, 109, 951; 1940, **62**, 667, 673, 977, 1514, 1963, 2327, 2606, 2813, 3208; 1941, **63**, 545, 1758, 2479.

-dibenzfuran, and -dibenzthiophen, but in these cases lithium hydride is then lost :



Aryl ethers, thioethers, and amines are all metalated by lithium compounds in the *ortho*-positions; triphenylamine is exceptionally attacked in the *meta*-position and thioanisole in the side-chain. In the attempted preparation of anisyl-lithium from *p*-bromoanisole, the product as formed metalated the unchanged ether to $\text{MeO} \cdot \text{C}_6\text{H}_3\text{BrLi}$.⁹³

These *ortho*-metalations have been extensively studied in the dibenzfuran,



dibenzthiophen, and carbazole series, where they open up position 1, the normal locus of substitution being 3 (I.). Furan is readily substituted in the α -position, and furyl-sodium reversibly metalates thiophen. The presence of acidic hydrogen in the nucleus does not prevent *ortho*-metalation, by butyl-lithium, of arylcarbinols, arylamines, and phenols.

The Grignard reagent can effect similar substitutions under extreme conditions.⁹⁴

Fluorobenzene and phenyl-lithium afford diphenyl surprisingly rapidly, but if benzophenone is added to the reaction mixture in place of water the product is diphenyl-*o*-diphenylcarbinol,⁹⁵ and it appears that the first stage is $\text{o-C}_6\text{H}_4\text{FLi}$ in which the fluorine atom is now labile and reacts with more phenyl-lithium, giving *o*-diphenyl-lithium.

Bromine or iodine may be replaced by lithium, $\text{ArBr} + \text{BuLi} \longrightarrow \text{ArLi} + \text{BuBr}$, in mono- and poly-cyclic aryl halides, halogenated ethers, and amines, and in derivatives of pyridine, quinoline, dibenzfuran, and carbazole.^{93, 95, 96, 97} The reactions are sometimes reversible and are influenced by the nature of the solvent and the lithium compound. *p*-Bromoaniline, by the successive action of butyl-lithium (3 mols.) and phenyldichloroarsine, gave phenyldi-*p*-aminophenylarsine. Apparently simple metalations or coupling reactions are sometimes two-stage processes involving metal-halogen "interconversion": $\text{PhBr} + \text{BuLi} \longrightarrow \text{PhLi} + \text{BuBr} \longrightarrow \text{PhBu} + \text{LiBr}$; and $\text{MeO} \cdot \text{C}_6\text{H}_4\text{Br} + \text{BuLi} \longrightarrow \text{MeO} \cdot \text{C}_6\text{H}_4\text{Li}$; $\text{MeO} \cdot \text{C}_6\text{H}_4\text{Li} + \text{MeO} \cdot \text{C}_6\text{H}_4\text{Br} \longrightarrow \text{MeO} \cdot \text{C}_6\text{H}_3\text{BrLi}$. Organolithium compounds can catalyse a similar interconversion between dibutylmercury and iodobenzene: $2\text{PhLi} + \text{Bu}_2\text{Hg} \longrightarrow 2\text{BuLi} + \text{Ph}_2\text{Hg}$; $2\text{BuLi} + 2\text{PhI} \longrightarrow 2\text{PhLi} + 2\text{BuI}$.

Miscellaneous.—Unsymmetrical lead compounds have been prepared :⁵⁴

⁹³ G. Wittig, U. Pockles, and H. Dröge, *Ber.*, 1938, **71**, 1903.

⁹⁴ F. Challenger and S. A. Miller, *J.*, 1938, 894; F. Challenger and G. M. Gibson, *J.*, 1940, 305.

⁹⁵ G. Wittig and U. Pockels, *Ber.*, 1939, **72**, 88; G. Wittig and G. Fuhrmann, *Ber.*, 1940, **73**, 1197, 1193 (with G. Pieper).

⁹⁶ H. Gilman *et al.*, *J. Amer. Chem. Soc.*, 1939, **61**, 106, 951, 1371; 1940, **62**, 346, 348, 1843, 1847, 1940, 1963, 2327, 2606, 2813; 1941, **63**, 545, 1441, 1443, 1553, 2844.

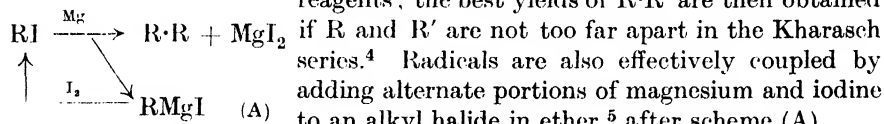
⁹⁷ H. Gilman and S. M. Spatz, *ibid.*, 1940, **62**, 446.

$\text{Ar}_3\text{PbBr} \longrightarrow \text{Ar}_3\text{PbNa} \longrightarrow \text{Ar}_3\text{PbR}$, and bismuth compounds analogously.⁹⁸ Diphenyliodonium iodide yields with mercury diphenylmercury, and with antimony and sodium sulphide, triphenylantimony sulphide.⁹⁹ The addition of sodium to polycyclic aromatic nuclei is greatly accelerated in dimethyl ether or ethylene glycol dimethyl ether.¹

Synthetic Applications.

sec.- and *tert.*-Alkyl-lithium,² pyridyl- and quinolyl-lithium,⁹⁷ and pyridylmagnesium compounds³ are now available.

The silver halide method for *hydrocarbons*, $\text{RMgX} + \text{AgX} \longrightarrow \text{RAg} + \text{MgX}_2$; $2\text{RAg} \longrightarrow \text{R}\cdot\text{R} + 2\text{Ag}$, can be applied to a mixture of Grignard reagents; the best yields of $\text{R}\cdot\text{R}'$ are then obtained if R and R' are not too far apart in the Kharasch series.⁴ Radicals are also effectively coupled by adding alternate portions of magnesium and iodine to an alkyl halide in ether,⁵ after scheme (A).



When an aryl halide is added to phenylmagnesium bromide containing a little cobalt chloride, diphenyl is produced in good yield along with polyaryl corresponding to the halide. Phenyl-lithium reacts similarly, and when an alkyl halide is used a mixture of alkane and alkylene takes the place of polyaryl. The process is formulated as a chain reaction: $\text{PhMgBr} + \text{CoCl}_2 \longrightarrow \text{PhCoCl} + \text{MgClBr}$; $2\text{PhCoCl} \longrightarrow \text{Ph}_2 + 2\text{CoCl}$; $\text{CoCl} + \text{ArBr} \longrightarrow \text{CoClBr} + \text{Ar}$ (polymerises).⁶

*neo*Pentyl iodide, inaccessible by simpler methods owing to molecular rearrangements, has been obtained from the chloride: $\text{RCl} \longrightarrow \text{RMgCl} \longrightarrow \text{RHgCl} \longrightarrow \text{RI}$.⁷

The preparation of *alcohols* and especially *phenols* by the action of oxygen on organolithium compounds has been carefully studied.⁸ Aryl derivatives of aluminium,⁴² indium,^{9(p.136)} and thallium^{11(p.136)} also give phenols. Small quantities of heavy metal halides profoundly influence the interaction of the Grignard reagent with ketones, often in the direction of pinacol formation.⁹

Functional groups show the following order of diminishing reactivity

⁹⁸ H. Gilman and H. L. Yablunsky, *J. Amer. Chem. Soc.*, 1941, **63**, 212.

⁹⁹ R. B. Sandin, F. T. McClure, and F. Irwin, *ibid.*, 1939, **61**, 2944.

¹ N. D. Scott, J. F. Walker, and V. L. Hansley, *ibid.*, 1936, **58**, 2442.

² H. Gilman, F. W. Moore, and O. Baine, *ibid.*, 1941, **63**, 2479.

³ J. Overhoff and W. Proost, *Rec. Trav. chim.*, 1938, **57**, 179; W. Proost and J. P. Wibaut, *ibid.*, 1940, **59**, 971.

⁴ J. H. Gardner, L. Joseph, and F. Gollub, *J. Amer. Chem. Soc.*, 1937, **59**, 2583; L. Joseph and J. H. Gardner, *J. Org. Chem.*, 1940, **5**, 61; E. A. Bickley and J. H. Gardner, *ibid.*, p. 126.

⁵ J. W. H. Oldham and A. R. Ubbelohde, *J.*, 1938, 201.

⁶ M. S. Kharasch and E. K. Fields, *J. Amer. Chem. Soc.*, 1941, **63**, 2316; M. S. Kharasch and W. B. Reynolds, *ibid.*, p. 3239.

⁷ F. C. Whitmore, E. L. Wittle, and B. R. Harriman, *ibid.*, 1939, **61**, 1585.

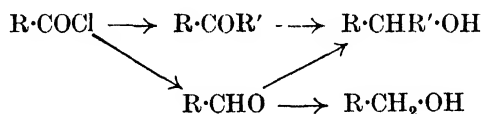
⁸ E. Müller and T. Töpel, *Ber.*, 1939, **72**, 273.

⁹ M. S. Kharasch *et al.*, *J. Amer. Chem. Soc.*, 1941, **63**, 2305, 2308, 2316.

towards the Grignard reagent: CHO, COMe, COF, COPh, COCl, COBr, CO₂Et, CN.¹⁰ It is inferred from the order of the acid halides that they react first at the carbonyl group. Towards ditolylmercury, on the other hand, which is inert to simple carbonyl compounds, the reactivity rises from Ph·COF to Ph·COI.⁴⁸

In many comparative experiments *aldehydes* were obtained in better yields from ethyl orthoformate than from disubstituted formamides,¹¹ which tend to give amines, $R_2N\cdot CHO + 2R'MgX \longrightarrow R_2N\cdot CHR'_2 + MgO + MgX_2$; this side reaction is less prevalent in the analogous synthesis of *ketones*. Organocadmium compounds are recommended for the preparation of ketones from acid chlorides or anhydrides.^{43, 12} Chloromercurifurans yield acetylfurans with keten.¹³ Highly substituted benzoyl chlorides with methylmagnesium iodide may give the related benzil¹⁴ or dibenzoylmethane.¹⁵

Acid chlorides can give primary or secondary in place of tertiary alcohols¹⁶ with the Grignard reagent $R'MgX$, which suffers compensatory dehydrogenation to olefin:



In these reductions, favoured by chain-branching in either or especially both reactants, the secondary alcohol arises mainly from the aldehyde, which was obtained in quantity in exceptional cases. A further product may be the ketone COR_2 or the related carbinol.¹⁷ A. D. Petrov¹⁸ has studied the production of ketones COR_2 and $CORR'$ from esters and, usually, *tert.*-butylmagnesium chloride. Salts such as $C_6H_{11}\cdot CO_2\cdot MgBr$ react somewhat similarly with, *inter alia*, cyclohexylmagnesium bromide, which gives some cyclohexanol.¹⁹ M. Tuot discusses in general terms secondary reactions between the Grignard reagent and esters or ketones.²⁰

¹⁰ C. E. Entemann and J. R. Johnson, *J. Amer. Chem. Soc.*, 1933, **55**, 2900.

¹¹ L. I. Smith and M. Bayliss, *J. Org. Chem.*, 1941, **6**, 437; N. Maxim and R. Mavrodineanu, *Bull. Soc. chim.*, 1935, **2**, 591; 1936, **3**, 1084; P. L. Couturier, *Compt. rend.*, 1937, **205**, 800; *Ann. Chim.*, 1938, **10**, 559.

¹² P. L. de Benneville, *J. Org. Chem.*, 1941, **6**, 462.

¹³ W. J. Chute, W. M. Orchard, and G. F. Wright, *ibid.*, p. 157.

¹⁴ R. C. Fuson and J. Corse, *J. Amer. Chem. Soc.*, 1938, **60**, 2063.

¹⁵ W. E. Ross and R. C. Fuson, *ibid.*, 1937, **59**, 1508; R. C. Fuson, J. H. Van Campen, and D. E. Wolf, *ibid.*, 1938, **60**, 2269; cf. D. W. Cowie and D. T. Gibson, *J.*, 1934, 46.

¹⁶ F. C. Whitmore *et al.*, *Rec. Trav. chim.*, 1938, **57**, 562; *J. Amer. Chem. Soc.*, 1938, **60**, 2028, 2030, 2458, 2462, 2788, 2790, 2899; 1941, **63**, 2788.

¹⁷ A. D. Petrov and N. A. Roslova, *J. Gen. Chem. Russia*, 1940, **10**, 973.

¹⁸ *Ibid.*, 1937, **7**, 565, 570, 2665; 1938, **8**, 195, 199; *Bull. Soc. chim.*, 1936, **3**, 169; *Bull. Acad. Sci. U.R.S.S., Sér. Chim.*, 1938, 347.

¹⁹ M. Mousseron and R. Granger, *Compt. rend.*, 1937, **204**, 986.

²⁰ *Ibid.*, 1938, **206**, 1019, 1124; **207**, 1227.

The carbonation of lithium and magnesium compounds has been closely studied.²¹ With methylmagnesium iodide, carbon suboxide yields tri-acetylphloroglucinol.²²

Phenylhydrazones suffer reductive fission by the Grignard reagent, giving ketimines and thence ketones or anils. Those of aldehydes may first undergo normal addition to the double bond, and the Fischer indole synthesis may occur with those of ketones. Phenylhydrazides of acids afford primarily hydrazones, $R \cdot CO \cdot NH \cdot NPh \longrightarrow CRR' \cdot N \cdot NPh$.²³

Amines have been effectively prepared from *o*-methylhydroxylamine by organo-lithium or -magnesium compounds,²⁴ from monochloroamine by magnesium, zinc, or lithium derivatives, and in smaller yield by zinc compounds from nitrogen chloride.²⁵ With arylmercury acetates, nitrosyl chloride yields *nitroso-compounds*.²⁶ Many metallic aryls yield *diazonium nitrates* with (best) $NO + N_2O_3$.^{12(p.186), 47}

Abnormal Reactions.—The Grignard reagent from, *e.g.*, cinnamyl chloride, is believed to be a mixture of $CHPh \cdot CH \cdot CH_2 \cdot MgCl$ and $CH_2 \cdot CH \cdot CHPh \cdot MgCl$, and affords derivatives of both types.^{27, 28} The frequent production of *o* (and more rarely *p*)-tolyl compounds from benzylmagnesium chloride²⁷ is paralleled by the behaviour of lithium, aluminium, zinc, cadmium, and mercury derivatives.²⁹ Only leading references can be given to apparently pinacolic changes frequently observed in the action of the Grignard reagent on ethylene oxides,³⁰ diketones,³¹ and chloro-ketones, -esters, or -acid chlorides.³² Propiophenoneoxime with phenylmagnesium bromide gives the amino-alcohol $HO \cdot CPh_2 \cdot CHMe \cdot NH_2$.³³

Fission of allyl aryl ethers take place at 50° : $C_3H_5 \cdot OAr + RMgX \longrightarrow C_3H_5R + ArO \cdot MgX$. The smooth formation of C_3H_5R contrasts with the production of mixtures of paraffins and olefins at higher temperatures from alkyl aryl ethers. Diphenyl ether with phenylsodium yields 2-hydroxy-

²¹ H. Gilman and P. R. Van Ess, *J. Amer. Chem. Soc.*, 1933, **55**, 1258; M. Tuot, *Compt. rend.*, 1939, **208**, 1026.

²² J. H. Billman and C. M. Smith, *J. Amer. Chem. Soc.*, 1939, **61**, 457.

²³ P. Grammaticakis, *Compt. rend.*, 1936, **202**, 1289; 1937, **204**, 502; 1938, **206**, 1307; 1939, **208**, 287, 1910, 1998; **209**, 1317.

²⁴ N. I. Scheverdina and K. A. Kotscheschkov, *J. Gen. Chem. Russia*, 1938, **8**, 1825.

²⁵ G. H. Coleman *et al.*, *J. Amer. Chem. Soc.*, 1928, **50**, 1193; 1929, **51**, 567; 1933, **55**, 2075, 3001, 3669; 1934, **56**, 965, 1381; 1936, **58**, 27; 1937, **59**, 1896; 1941, **63**, 1692.

²⁶ L. I. Smith and F. L. Taylor, *ibid.*, 1935, **57**, 2460.

²⁷ *Ann. Reports*, 1932, **29**, 145.

²⁸ W. G. Young *et al.*, *J. Amer. Chem. Soc.*, 1936, **58**, 289, 441; 1938, **60**, 900; 1939, **61**, 12; 1941, **63**, 2113.

²⁹ H. Gilman and F. Breuer, *ibid.*, 1934, **56**, 1127; H. Gilman and J. F. Nelson, *ibid.*, 1939, **61**, 741.

³⁰ F. H. Norton and H. B. Hass, *ibid.*, 1936, **58**, 2147; J. W. Cook, C. L. Hewett, and C. A. Lawrence, *J.*, 1936, 71.

³¹ R. Roger and A. McGregor, *J.*, 1934, 442.

³² *Idem*, *ibid.*, p. 1850; J. S. W. Boyle, A. McKenzie, and W. Mitchell, *Ber.*, 1937, **70**, 2153; Z. Földi and I. Demjen, *Ber.*, 1941, **74**, 930.

³³ K. N. Campbell and J. F. McKenna, *J. Org. Chem.*, 1939, **4**, 198.

diphenyl by rearrangement following *o*-metalation.³⁴ Organosodium compounds may react with esters: $\text{RNa} + \text{R}'\cdot\text{CO}_2\text{R}'' \longrightarrow \text{R}'\cdot\text{CO}_2\text{Na} + \text{RR}''$.³⁵

T. S. S.

4. POLYSACCHARIDES.

Pectic Substances, Mucilages, Gums.

The widespread distribution of polyglucoses and the fundamental importance of their rôle in plant and animal life led to extended studies being made of the constitutions of starch, glycogen, cellulose and the like, somewhat to the neglect perhaps of the many other types of polysaccharides which occur in Nature. The view thus became current that the most favoured type of union of monosaccharide units in the elaboration of polysaccharides was the 1 : 4-glycosidic type, with the occasional appearance of 1 : 6-glycosidic linkages. In recent years, however, a body of fact has grown up which shows that other types of glycosidic linkage are by no means the rarity they were first supposed to be and that indeed 1 : 2-, 1 : 3- and 1 : 5-linkages are found in many natural polysaccharides. This becomes increasingly clear as more and more of those carbohydrates ill-defined as gums, mucilages, pectins and pectic substances are submitted to examination.

There is a real need for a logical system of nomenclature for this great group of carbohydrates which will be both comprehensive and exclusive and which will embrace the carbohydrate products of both the plant and the animal kingdom. When our knowledge of the chemistry of these substances is more advanced than it is at present it may be possible to derive a system of classification based upon constitutional affinities rather than on physical properties, biological function or pharmaceutical or industrial application.

In a review of this group one cannot better begin than with a consideration of the so-called pectins. It seems now to be accepted that pectins from various sources are mixtures of polysaccharides in which the chief constituent is pectic acid (a polygalacturonic acid). With the pectic acid is associated a polyarabinose (araban) and frequently a polygalactose (galactan or galactogen).

The view of Ehrlich and others that in pectin the arabinose is in chemical combination with pectic acid is no longer tenable, nor does it appear to be true that in pectins containing galactose as well as arabinose, the latter two units are combined together as galactaraban.¹

Pectin.—The substance properly called pectin is composed exclusively of *d*-galacturonic acid residues, which may in part be esterified with methyl alcohol. Pectic acid, produced by acid hydrolysis of pectin, is a degraded

³⁴ A. Lüttringhaus and (Frl.) G. von Sääf, *Ber.*, 1938, **71**, 1673; *Angew. Chem.*, 1938, **51**, 915; *Annalen*, 1939, **542**, 241; V. Grignard and J. Ritz, *Bull. Soc. chim.*, 1936, **3**, 1181.

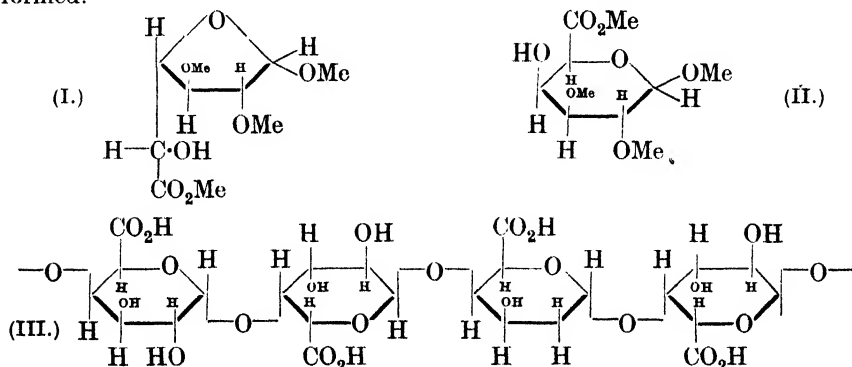
³⁵ H. F. Tseou and Y. T. Wang, *J. Chinese Chem. Soc.*, 1937, **5**, 224; H. F. Tseou and T. S. Chow, *ibid.*, 1939, **7**, 27; J. R. Roland and S. M. McElvain, *J. Amer. Chem. Soc.*, 1937, **59**, 132.

¹ E. L. Hirst and J. K. N. Jones, *J.*, 1938, 496; 1939, 452.

and demethylated product, but still contains at least ten galacturonic acid residues.² The earlier conception of the linkages between the galacturonic acid constituents of pectic acid as being 1 : 4-glycosidic is now confirmed by the successful methylation and hydrolysis of pectic acid from two sources, namely, citrus pectin and strawberry pectin. Strawberry pectic acid has been examined by G. H. Beavan and J. K. N. Jones,³ and citrus pectic acid by S. Luckett and F. Smith,⁴ and it appears that in these two compounds the fundamental features of the chemical structure are identical.

Technical difficulties were experienced in the methylation of pectic acid, and in order to prepare the methyl ester of methylated pectic acid it was necessary to treat the pectic acid successively by the methyl sulphate-sodium hydroxide, the thallium and the methyl iodide-silver oxide methods. The fully methylated pectic acid so obtained was resistant to ordinary hydrolytic procedure. In the first instance methanolysis was achieved only at an elevated temperature and under pressure and the chief product was recognised as the methyl ester of 2 : 3-dimethyl methylgalactofururonoside (I).

The presence of the furanose ring in (I) might suggest that the galacturonic residues in pectic acid are also furanose in form. This view, however, is not supported by the high positive rotation of pectic acid, its stability towards hydrolytic agents and the ease of hydrolysis of the furanose form of methylated galacturonic acid. It is therefore concluded that the galacturonic acid units in pectic acid are pyranose units linked through positions 1 and 4 and that a change of ring form to (I) takes place under the exceptional conditions of hydrolysis. This conclusion found ample support in the observations (i) that 2 : 3-dimethyl galacturonic acid shows a marked tendency to form a methylfuranoside when treated with hot methyl-alcoholic hydrogen chloride and (ii) that when the methyl ester of methylated pectic acid is treated with methyl-alcoholic hydrogen chloride, not in a sealed tube, but by boiling under reflux for a prolonged period, partial hydrolysis occurs and the methyl ester of 2 : 3-dimethyl methylgalactopyruronoside (II) is formed.⁴



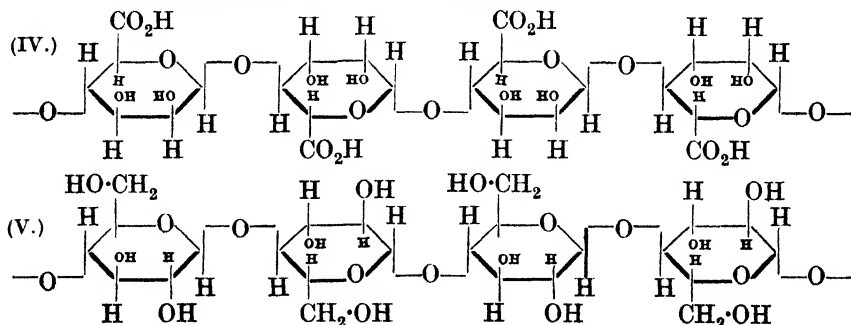
² *Ann. Reports*, 1937, **34**, 300.

³ *Chem. and Ind.*, 1939, **58**, 363.

⁴ F. Smith, *ibid.*, p. 363; S. Luckett and F. Smith, *J.*, 1940, 1106, 1114, 1506.

The consensus of opinion therefore favours the formulation of pectic acid as (III), where the linkages between pyranose units are α -1 : 4-glycosidic. The methyl ester of the methylated pectic acid examined by Luckett and Smith showed a molecular weight (by osmotic pressure measurement) corresponding to a chain length of 13 galacturonic acid residues. Nevertheless an end-group (the methyl ester of a trimethyl methylgalacturonoside) was not detected among the cleavage fragments and the possibility that methylated pectic acid is composed of galacturonic acid residues arranged in a loop must be envisaged.

Alginic Acid.—A substance which exhibits many physical and chemical properties analogous to those of pectic acid is alginic acid, which as a salt occurs in certain seaweeds in association with other polysaccharides such as fucosan (a polyfucose). Earlier work had shown that alginic acid was probably built up entirely of *d*-mannuronic acid residues, although its extreme resistance to hydrolysis made a quantitative conversion into *d*-mannuronic acid not possible of achievement. Pectic acid is degraded by methyl-alcoholic hydrogen chloride to *d*-galacturonic and a pectic acid of lower molecular size,⁵ and in similar fashion alginic acid gives *d*-mannuronic acid and degraded alginic acid. E. L. Hirst, J. K. N. Jones, and W. O. Jones⁶ found that degraded alginic acid was more amenable to chemical treatment than the original acid and they were able successfully to methylate it by the thallium method. Methylated degraded alginic acid showed an even greater resistance to hydrolytic reagents than does methylated pectic acid, but from it there was ultimately obtained, by drastic treatment with methyl-alcoholic hydrogen chloride, the methyl ester of 2 : 3-dimethyl methyl-*d*-mannuronide. The disposition of the methyl groups at C₂ and C₃ was established by oxidative processes and a choice between pyranose and furanose ring forms favoured the former because of the extreme stability of alginic acid and its large negative rotation. At least half, and probably the whole, of the molecule of alginic acid is therefore represented by (IV), in which the linkages are shown as β -1 : 4-glycosidic.



It is worthy of note that both pectic acid (III) and alginic acid (IV) conform exactly to type with the geometrical pattern, not of starch, but of

⁵ S. Morell, L. Baur, and K. P. Link, *J. Biol. Chem.*, 1934, **105**, 1.

⁶ *J.*, 1939, 1880.

cellulose (V), and this despite the fact that the linkages in pectic acid are α -glycosidic. It is of interest in this connection to find that threads prepared from alginic acid give a typical X-ray fibre diagram, and the view is expressed that this polysaccharide is to be considered as a link between the homopolar celluloses and the heteropolar proteins.⁷

A characteristic feature of polysaccharides such as cellulose, pectic acid, alginic acid, starch, lies in what might be termed the simplicity of their structures. Each is formed from the union of monosaccharide residues of one and the same type and the repeating units of the polysaccharides are unbranched chains of these residues. Other examples of this "simple" type may be called to mind in which the glycosidic unions are not necessarily 1 : 4. Among the polyglucoses there are, for instance, the dextrans synthesised by *Leuconostoc dextranicum*,⁸ *B. vermiforme*,⁹ and the water-soluble glucosan from barley roots,¹⁰ each of which consists of a terminated chain of glucose units combined by α -1 : 6-glycosidic links. A polyglucose has been extracted from *Laminaria cloustoni* (alginic acid is obtained from *L. digitata*), which displays an unusual type of glucosidic linkage. The polysaccharide when methylated and hydrolysed yields 2 : 4 : 6-trimethyl glucopyranose and must therefore consist of glucose residues united by 1 : 3-glycosidic linkages. Moreover, the small negative rotation of laminarin suggests that these linkages are of the β -type.¹¹ Laminarin appears to be the first known example of a polysaccharide in which C_3 of glucose is involved in the glycosidic linkage, although, as we shall see, the 1 : 3-linkage appears to be favoured when the units concerned are of galactose.

Very recently W. Z. Hassid, M. A. Joslyn, and R. M. McCready¹² have contributed another example of a polyglucose in which the glycosidic linkages are 1 : 3. This is an insoluble polysaccharide obtained from baker's yeast and the fully methylated product on hydrolysis gives rise to 2 : 4 : 6-trimethyl glucose only.

Agar.—The physical properties of agar-agar, the gelatinous extract of certain East Indian sea-weeds, for long impeded its accurate chemical investigation, but in 1937 E. G. V. Percival and J. C. Somerville were able to make out the main features of its structure by an application of the methylation method.¹³ The chief product of the hydrolysis of methylated agar was shown to be 2 : 4 : 6-trimethyl *d*-galactopyranose, a demonstration that methylated agar consisted in part at least of *d*-galactose linked by 1 : 3-glycosidic linkages. Moreover, it appeared likely that these linkages were of the β -type. The parallelism between agar and that other sea-weed product, laminarin, is obvious. But agar proved not to have so simple a structure as the above observations might suggest. It seemed, for instance,

⁷ E. Heen, *Tids. Kjem.*, 1937, 17, 127.

⁸ S. Peat, E. Schlüchterer, and M. Stacey, *J.*, 1939, 581.

⁹ W. D. Daker and M. Stacey, *J.*, 1939, 585.

¹⁰ W. Z. Hassid, *J. Amer. Chem. Soc.*, 1939, 61, 1223.

¹¹ V. C. Barry, *Sci. Proc. Roy. Dublin Soc.*, 1939, 20, 59; 1941, 22, 423.

¹² *J. Amer. Chem. Soc.*, 1941, 63, 295. ¹³ *J.*, 1937, 1615.

that some at least of the galactose residues were esterified with sulphuric acid, for commercial agar always contains sulphate, although this is lost in the processes of acetylation or methylation (cf. C. Neuberg and C. H. Schweitzer¹⁴). Again, N. W. Pirie¹⁵ made the noteworthy observation that *l*-galactose as well as *d*-galactose may be recognised among the acetolysis products of agar. In this case the *l*-galactose might have been a factitious product of the action of the acetolysing agents on *d*-galactose, but when later a derivative of *l*-galactose was found among the hydrolysis products of methylated agar, it became clear that *l*-galactose was an integral part of the polysaccharide.¹⁶ The methylated derivative of *l*-galactose displayed a further unusual feature in that it contained a 3 : 6-anhydro (or hydrofuranol) ring, the first 3 : 6-anhydro-sugar to be obtained from a natural source. The question arose as to whether this 3 : 6-anhydro-*l*-galactose was in fact an original constituent of agar, as it was always apparent that the 3 : 6-anhydro-ring might have been introduced during the hydrolysis of the sulphuric ester groupings of agar. Inasmuch as the hydrolysis of a sugar sulphonic ester is invariably accompanied by anhydro-ring formation it might be conjectured that the hydrolysis of a sulphuric ester would be accompanied by a similar effect. Percival¹⁷ has now presented clear evidence that the alkaline hydrolysis of methyl galactoside 6-sulphate leads to the formation of 3 : 6-anhydromethylgalactoside, and there is no longer reason to doubt that the anhydro-*l*-galactose is the hydrolytic product of a residue of *l*-galactose 6-sulphate in agar.

During a preparation of methylated agar, W. G. M. Jones and S. Peat¹⁸ purified the product by dialysis in aqueous acid solution and demonstrated the presence of carboxylic acid groups in the final product. Among the products of hydrolysis of this methylated polysaccharide acid there were detected tetramethyl *d*-galactopyranose and 2 : 5-dimethyl 3 : 6-anhydro-*l*-galactonic acid. A carboxylic acid has not hitherto been detected in agar and the *l*-galactonic acid is considered to be an artifact produced from a 3 : 6-anhydro-*l*-galactose residue by air oxidation during the preparation.

After a survey of the available experimental data, it seems that the constitution of agar is best represented by the formulation (VI). The repeating unit is represented as a chain of nine *d*-galactopyranose residues terminated at the reducing end by one residue of *l*-galactose. The linkages between the *d*-galactose members are 1 : 3-glycosidic, but the *l*-galactose residue is attached to the chain through position 4 and not through position 3. Further, the *l*-galactose residue is esterified with sulphuric acid at C₆.

In the course of methylation, the sulphuric acid residue is lost and a 3 : 6-anhydro-ring appears in the *l*-galactose member (VII). It has been

¹⁴ *Monatsh.*, 1937, **71**, 46.

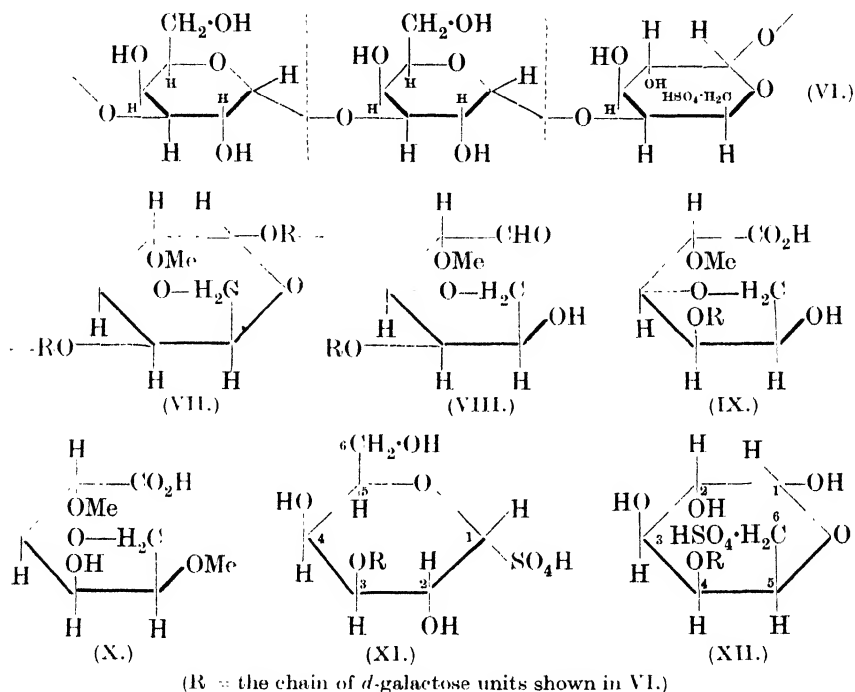
¹⁵ *Biochem. J.*, 1936, **30**, 369.

¹⁶ S. Hands and S. Peat, *Chem. and Ind.*, 1938, 937; *Nature*, 1938, **142**, 797; E. G. V. Percival, J. C. Somerville, and I. A. Forbes, *ibid.*, p. 797; I. A. Forbes and E. G. V. Percival, *J.*, 1939, 1846.

¹⁷ E. G. V. Percival and T. H. Soutar, *J.*, 1940, 1475; R. B. Duff and E. G. V. Percival, *J.*, 1941, 830.

¹⁸ *J.*, 1942, 225.

shown¹⁹ that anhydro-glycosides of the type (VII) are exceedingly sensitive to acid, and if acid conditions supervened during the preparation of methylated agar, the *aldehyde*-form (VIII) would result and would readily pass, by air oxidation, into the acid (IX). This sequence of changes explains the isolation of 2 : 5-dimethyl 3 : 6-anhydro-*l*-galactonic acid (X).



The fact is stressed that, whereas the *d*-galactose residues of agar are mutually combined by 1 : 3-linkages, the *l*-galactose residue is attached to the chain through position 4, and it may be significant in regard to the biological synthesis of this polysaccharide that *d*-galactose 1-sulphate substituted at C₃ (XI) is convertible by a simple intramolecular oxidation and reduction change into *l*-galactose 6-sulphate substituted at C₄ (XII). It appears possible that *d*-galactose 1-sulphate plays a similar part in the synthesis of agar to that played by glucose 1-phosphate in the synthesis of starch.²⁰

Snail Galactogen.—It has recently been shown that another polysaccharide exists (and this is of animal origin) in which the *d*- and the *l*-form of galactose are both present (see also ref. 45). It is the galactogen which occurs together with glycogen in the albumin glands of the vineyard snail, *Helix pomatia*, and D. J. Bell and E. Baldwin²¹ have demonstrated the presence in it of

¹⁹ W. N. Haworth, J. Jackson, and F. Smith, *J.*, 1940, 625.

²⁰ C. S. Hanes, *Proc. Roy. Soc.*, 1940, B, 128, 421; 129, 174.

²¹ *J.*, 1941, 125.

l-galactose inasmuch as *dl*-galactobenziminazole has been prepared from the products of its hydrolysis. An earlier examination of the galactogen had revealed the fact that it was differently constituted from most of the then known polyoses. Thus hydrolysis of the methylated polysaccharide yielded a mixture of tetramethyl *d*-galactopyranose and 2:4-dimethyl *d*-galactopyranose and no trimethyl galactose was found.²² The absence of the last-named substance meant that the repeating unit could not consist simply of an unbranched chain of galactose residues. An example is thus afforded of a new structure-pattern in natural polysaccharides. The relative proportion of tetra- and di-methyl galactose was such that the repeating unit of galactogen could be formulated as (XIIIa) or (XIIIb).



It will be convenient to represent the polysaccharides in this diagrammatic manner, particularly in the formulation of the more complex types. In (XIII), G represents a residue of galactopyranose, a stroke indicates a glycosidic link, and the numerals, the points of attachment of the glycosidic linkage. It is seen that in the repeating unit of galactogen there are four terminal galactose residues. One of these (it cannot be determined which) is *l*-galactose, the remainder are of *d*-galactose. The galactogen is non-reducing, and is therefore unlikely to be represented by the small unit (XIII), which has one free reducing group for seven galactose members. (XIII) is in fact the repeating unit and galactogen must be an aggregate of such units, analogous to the aggregation of repeating units in starch.

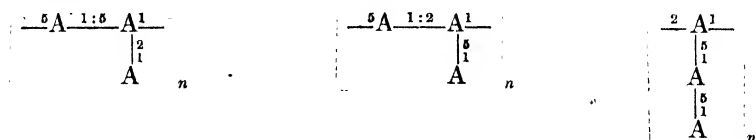
It is becoming evident that polysaccharides constituted of branched-chain repeating units are of common occurrence, and this is well illustrated by the arabans which are found in constant association with pectic acid in pectic substances. Before turning to consider these, however, it is worthy of note that the ϵ -galactan of larch wood has been shown to consist of an araban and a polygalactose. The latter after methylation and hydrolysis gives an equimolecular mixture of tetramethyl-, 2:4-dimethyl- and a trimethyl-galactopyranose, an indication that this polygalactose also is constituted of branched-chain repeating units.²³

Arabans.—Hirst and Jones¹ in an approach to the problem of the phytochemical origin of the pentose sugars instituted a comparison of the structures of the associated hexose and pentose units present in pectic substances. An araban was isolated from the pectic substance of the peanut and in contrast with the polygalacturonic acid with which it was associated, the araban was easily hydrolysable, was constituted solely of *l*-arabofuranose residues, and its repeating unit was of the branched-chain type. Hydrolysis of the methylated araban gave rise to three products in equimolecular proportions, namely, 2:3:5-trimethyl *l*-arabinose, 2:3-dimethyl *l*-arabinose, and 3-methyl *l*-arabinose. The first of these must of course exist in

²² E. Baldwin and D. J. Bell, *J.*, 1938, 1461.

²³ E. L. Hirst, J. K. N. Jones, and W. G. Campbell, *Nature*, 1941, 147, 25.

the araban in the furanose form and although the dimethyl and monomethyl arabinoses could exist in either pyranose or furanose forms, the furanose form is favoured because of the extreme ease of complete hydrolysis of the araban and its strong laevorotation. The latter property also points to the glycosidic linkages being of the α -type. Repeating units of the types shown in (XIV), or combinations of these, would satisfy the experimental observations.



(XIV; A = an α -arabofuranose residue.)

Later it was shown that the same araban is a constituent of apple pectin²⁴ and citrus pectin.²⁵ In each of these a galactan was present in addition to pectic acid.

There is a close chemical relationship between *d*-galactose, *d*-galacturonic acid and *l*-arabinose, and the almost invariable association together in nature of polygalactoses, polygalacturonic acids and polyarabinoses suggests a common biological origin or interconversion. Nevertheless, it is not possible that the araban (XIV) is produced directly by the decarboxylation of pectic acid (III). On the one hand, the galacturonic acid residues are pyranose and are held in an unbranched chain by 1:4-links and, on the other, the arabinose units are furanose and are assembled in branched chains by 1:5- as well as by 1:2-linkages.

Although it does not invalidate the conclusions reached, it is desirable to mention that P. A. Levene, G. M. Meyer, and M. Kuna²⁶ do not agree that the galacturonic acid residues in pectic acid are pyranose and maintain that the rate of hydrolysis of the fully methylated pectic acid examined by them indicates a furanose structure and therefore that the union between the uronic acid residues is 1:5-glycosidic.

Mannans.—Although mannose does not occur free in Nature, polymannoses are wide-spread. Mannans are found principally as cell-wall constituents of hard plant seeds. Such mannans may be described as hemicelluloses (if the latter term is used to connote polysaccharides which appear to have a similar biological function to cellulose) and they are constituted on the cellulose model in the sense that mannopyranose residues are combined in chain formation by β -1:4-glycosidic linkages.

In yeast, however, there occurs a mannan which is differently constituted and in fact affords an example of a polysaccharide composed of branched chain repeating units like the arabans mentioned above. W. N. Haworth, R. L. Heath, and S. Peat,²⁷ extending an earlier investigation of W. N. Haworth, E. L. Hirst, and F. A. Isherwood,²⁸ have shown that the

²⁴ E. L. Hirst and J. K. N. Jones, *J.*, 1939, 454.

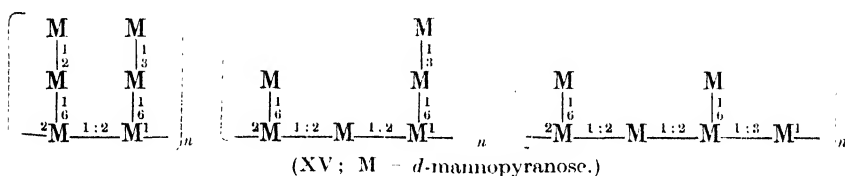
²⁵ G. H. Beavan, E. L. Hirst, and J. K. N. Jones, *J.*, 1939, 1865.

²⁶ *Science*, 1939, 89, 370.

²⁷ *J.*, 1941, 833.

²⁸ *J.*, 1937, 784.

repeating unit of yeast-mannan is an assemblage in a branched-chain structure of six *d*-mannopyrananose residues. The mannan was chemically homogeneous and constituted of mannopyranose units only and hydrolysis of the methylated mannan yielded a mixture of tetramethyl mannopyranose (2 mols.), 3 : 4 : 6-trimethyl mannose (1 mol.), 2 : 4 : 6-trimethyl mannose (1 mol.), and 3 : 4-dimethyl mannose (2 mols.). In addition, there was isolated 2 : 3 : 4-trimethyl mannose but only in an amount which was not greater than 3% of the weight of methylated polysaccharide. On the basis of these observations it is clear that the mannan is to be pictured as a central chain of mannose units with side chains radiating from this main chain. Some of the possible representations of the repeating unit are given in (XV).



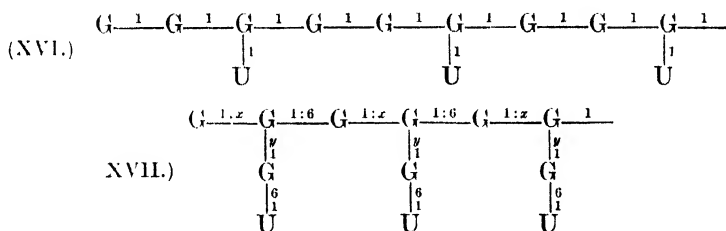
It is considered that the main chain is terminated and does not exist as a loop and that the small amount of 2 : 3 : 4-trimethyl mannose obtained represents the non-reducing end-group of this main chain. It is for this reason that main-chain glycosidic linkages are represented as (1 : 2) rather than as the alternative (1 : 6) and in consequence the attachment of the side-chains to the main chain is represented as 1 : 6-glycosidic. It will be noted that in yeast mannan three different types of glycosidic linkage obtain, namely, 1 : 2, 1 : 3 and 1 : 6.

Complex Polysaccharides.—The polysaccharides mentioned in the foregoing, with the exception of agar and snail galactogen, have been simple in the sense that each is constituted of only one type of monosaccharide building unit. But many polysaccharides exist in which this is by no means the case and in which there appears a variety not only of building units, but also of the modes of linkage of these units. Examples are presented particularly by the gums and mucilages of the plant world and the apparent lack of uniformity or plan of structure of these polysaccharides has necessitated caution in drawing any general conclusions. These investigations are by no means complete even in the case of a single gum or mucilage and only in the case of gum arabic has anything like a complete structural representation been made out.

The chief monosaccharide units which go to form the complex polysaccharides are the pentoses, *l*-arabinose and *d*-xylose; the methylpentoses, *l*-rhamnose and *l*-fucose; the hexoses, *d*-galactose and *d*-mannose; and the uronic acids, *d*-galacturonic and *d*-glucuronic acids. So far as is known, combined arabinose exists solely in the furanose form.

In illustration of the problems which have to be faced in the study of the complex polysaccharides and the difficulties which have to be overcome,

we will consider the case of gum arabic. F. Smith, in a series of five papers,²⁹ has described experiments on the basis of which it is now possible to formulate the structure of arabic acid with considerable accuracy of detail, although a complete picture cannot yet be presented. The total hydrolysis of arabic acid with mineral acid is a matter of considerable difficulty, but partial autohydrolysis occurs when the polysaccharide acid is boiled in water, with the liberation of *l*-arabinose, *l*-rhamnose, a disaccharide which was proved to be 3-galactosido-*l*-arabinose, and a resistant nucleus or core, degraded arabic acid. This nucleus, which retained the properties of a polysaccharide acid, was examined by the methylation method. Hydrolysis of methylated degraded arabic acid furnished tetramethyl galactose (1 mol); 2 : 3 : 4-trimethyl galactose (5 mols.); 2 : 4-dimethyl galactose (3 mols.) and 2 : 3 : 4-trimethyl glucuronic acid (3 mols.). The identification of these methylated derivatives shows that 1 : 6- and 1 : 3-glycosidic linkages are present and that the repeating unit of degraded arabic acid is of the branched-chain type discussed above. The minimum molecular size of degraded arabic acid is that of an assemblage of nine *d*-galactopyranose and three *d*-glucuronic acid residues and of these one galactopyranose residue and all the glucuronic acid residues constitute terminal groups. There must therefore be three branches from a main chain of galactose members and two possible modes of branching are shown in (XVI) and (XVII).



(The Reporter is responsible for the diagrammatic character of these formulations. G = *d*-galactopyranose; U = *d*-glucopyruronic acid. The glycosidic linkages where unspecified are either 1 : 6 or 1 : 3.)

The formulation (XVII) is preferred for several reasons. Arabic acid is known to yield by hydrolysis an aldobionic acid, 6-β-glucuronosidogalactose, and Smith has obtained from methylated degraded arabic acid the hexamethyl derivative of this aldobionic acid, which in turn yields 2 : 3 : 4-trimethyl galactose when it is hydrolysed. It follows that at least some of the side chains, and possibly all of them, consist of the aldobionic acid as shown in (XVII). Three of the five molecular proportions of 2 : 3 : 4-trimethyl galactose are thus accounted for by the side chains and consequently at least two of the glycosidic linkages in the main chain must be 1 : 6. These are shown in (XVII).

The existence of 1 : 3-linkages between galactose residues was proved

²⁹ F. Smith, *J.*, 1939, 744, 1724; J. Jackson and F. Smith, *J.*, 1940, 74, 79; F. Smith, *ibid.*, p. 1035.

when, by the further partial hydrolysis of degraded arabic acid, a disaccharide, 3-galactosidogalactose, was isolated. The 1:3-linkages must engage those galactose members of the main chain at which the side-chains are attached, that is, those galactose residues which give rise to 2:4-dimethyl galactose when methylated degraded arabic acid is completely hydrolysed. Were this not so, 2:4:6-trimethyl galactose would also appear in the hydrolysate. It has not yet been determined whether the 1:3-linkages are in the main chain or whether they form the attaching links of the side chains. If the main-chain linkages at (*x*) in (XVII) are 1:3, then the side chain linkages at (*y*) are 1:6, and vice versa.

The pattern of the repeating unit of the central nucleus having thus been made clear in all essential respects, it was possible to turn to the question of the constitution of arabic acid itself. It will be recalled that the production of degraded arabic acid by the autohydrolysis of arabic acid is accompanied by the liberation of *l*-rhamnose, *l*-arabinose and 3-galactosido-*l*-arabinose. It follows that in arabic acid these sugars must be glycosidically attached to the nucleus (XVII). The points of attachment are determined by a study of the products of hydrolysis of fully methylated arabic acid. These were shown to be 2:3:4-trimethyl *l*-rhamnose, 2:5-dimethyl and 2:3:5-trimethyl *l*-arabofuranose, 2:3:4:6-tetramethyl *d*-galactose, 2:4-dimethyl *d*-galactose, 2:3-dimethyl *d*-glucuronic acid, and 2:3:4-trimethyl *d*-glucuronic acid. It will be conceded that the separation and identification of these seven closely related substances represent a technical achievement of a very high order.

The inferences to be drawn from this analysis of methylated arabic acid may be set out as follows:

(1) The *l*-arabinose constituent appears to exist exclusively in the furanose form.

(2) The isolation of the whole of the rhamnopyranose and part of the arabofuranose as the trimethyl derivatives indicates that these sugars constitute terminal groups, as does that part of the galactose which yields tetramethyl galactopyranose.

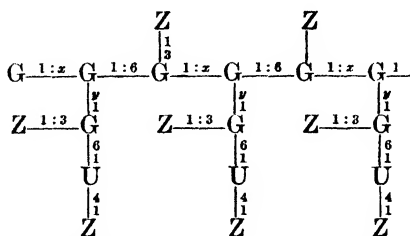
(3) Practically the whole of the glucuronic acid constituent is found as the 2:3-dimethyl derivative and therefore it is evident that, although this acid represents a terminal group in degraded arabic acid, it must represent an intermediate residue in arabic acid itself. In other words, the side chains of degraded arabic acid (XVII) are extended by the glycosidic attachment of a sugar residue (*Z*) at position 4 of each glucopyruronic acid residue.

(4) The residue (*Z*) will be itself terminated by *l*-rhamnopyranose, *l*-arabofuranose or *d*-galactopyranose.

(5) It is to be noted that no trimethyl galactose is found in the hydrolysate of methylated arabic acid, and it follows that not only does the glucuronic acid of degraded arabic acid carry an addendum, *Z*, but so also does the galactose of the side chain, and as 2:4-dimethyl galactose is the only dimethyl galactose isolated from methylated arabic acid, the attachment of (*Z*) must involve position 3 of each galactose residue in the side chains.

The same argument obviously applies to those galactose members of the main chain of degraded arabic acid which give rise 2 : 3 : 4-trimethyl galactose.

These deductions concerning the structure of arabic acid are expressed in the diagrammatic formula (XVIII).



(XVIII; G = *d*-galactopyranose, U = *d*-glucopyruronic acid,
 $x = 3$ or 6 and $y = 6$ or 3 respectively.)

The constituents of the addenda (Z) are known. They are clearly those sugars which are liberated during the autohydrolysis of arabic acid, namely, *l*-rhamnopyranose, *l*-arabofuranose and 3-galactosido-*l*-arabinose, but the individual disposition of these residues in the repeating unit has not yet been determined. To quote the author, "a portion of the arabinose constituent of arabic acid is isolated from methylated arabic acid as 2 : 5-dimethyl arabofuranose and this must therefore represent arabinose units which are interposed between the terminal groups of the side chains and the nucleus of degraded arabic acid. . . . It may well be that arabofuranose units are . . . interposed between the nucleus . . . and the terminal groups, rhamnopyranose and arabofuranose, and the resulting side chains would conform in type to that represented by 3-galactosido-arabinose."

Summarising briefly, the repeating unit of arabic acid has been shown to be a complex ramified structure composed of residues of *d*-galactose, *l*-arabinose, *l*-rhamnose and *d*-glucuronic acid. These residues are mutually combined by three different types of glycosidic linkage, namely, by 1 : 6-, 1 : 3-, and 1 : 4-linkages.

The properties and structural pattern of gum arabic are largely simulated by those of another plant gum, namely, the gum which is exuded on the bark of damson trees. The investigation of damson gum was begun in masterly fashion by E. L. Hirst and J. K. N. Jones.³⁰ Much progress has been made and the main features of the structure of the gum have been made out.

A comparison with gum arabic will be helpful in appreciating the constitution of damson gum. Three of the monosaccharide units of gum arabic are found also in damson gum. These are *d*-glucuronic acid, *d*-galactose and *l*-arabinose. The damson gum contains no rhamnose but instead *d*-mannose is shown to be a constituent. As with arabic acid, it is possible to degrade damson gum by partial hydrolysis and when submitted to this

³⁰ *J.*, 1938, 1174; 1939, 1482.

process *l*-arabinose is preferentially removed (at a rate suggesting its existence in the furanose form), and an acid polysaccharide (polysaccharide-A, corresponding to degraded arabic acid) remains. The repeating unit of polysaccharide-A is constituted essentially of *d*-galactose (2 mols.), *d*-glucuronic acid (1 mol.) and *d*-mannose (1 mol.). Later it was shown also to contain a little *d*-xylose (*ca.* 3%). One of the first fragments of gum arabic to be characterised was the aldobionic acid, 6-glucuronosido-galactose,³¹ and the implied greater stability of the glycosidic linkage in the aldobionic acids as compared with disaccharides has been confirmed by the persistence of such linkages during the hydrolysis of many polysaccharides containing uronic acid residues, and by the difficulty in hydrolysing polyuronides such as alginic acid. Damson gum is no exception, and the further hydrolysis of polysaccharide-A yielded among other products, an aldobionic acid of novel and unexpected constitution. The fully methylated aldobionic acid gave, when hydrolysed, equimolecular proportions of 2 : 3 : 4-trimethyl *d*-glucuronic acid and 3 : 4 : 6-trimethyl *d*-mannose. This fact, considered together with the negative rotation of the aldobionic acid, justifies its description as 2-β-*d*-glucopyruronosido-*d*-mannose.

Degraded arabic acid is composed of residues of galactose and glucuronic acid only, but polysaccharide-A contains in addition mannose and xylose. The nucleus of damson gum is of the branched-chain type and is possibly of a similar pattern to that of degraded arabic acid, inasmuch as the hydrolysis of methylated polysaccharide-A yields tetramethyl galactose (1 part), 2 : 3 : 4-trimethyl galactose (1 part), 2 : 4-dimethyl galactose (1 part), and 2 : 3 : 4-trimethyl glucuronic acid (1 part).

(Note : In the paper³⁰ the dimethyl galactose is described as 4 : 6, but it appears that, although some 4 : 6-dimethyl galactose is found, the major part of the dimethyl galactose is the 2 : 4-dimethyl, the 4 : 6- probably arising from under-methylation.³²)

These products are also obtained from methylated degraded arabic acid, but it will be observed that their relative proportions are not the same, and furthermore, there are obtained from methylated polysaccharide-A, 2 : 3-dimethyl glucuronic acid (1 part) and 2 : 3 : 4-trimethyl xylose ($\frac{1}{6}$ part) in addition to the above. Mannose derivatives must also be present, but these have not yet been identified.

It is clear, as the authors state, that it is impossible on the evidence available to make a unique decision as to the formulation of polysaccharide-A. Such a decision will have to wait upon the examination of the methylated undegraded gum which it is proposed to carry out. Nevertheless, the striking resemblances between the structures of the two gums most closely studied so far cannot fail to impress the observer.

Cherry gum has been examined by J. K. N. Jones.³³ It shows a relationship with damson gum, in so far as each gives by appropriate treatment

³¹ S. W. Challinor, W. N. Haworth, and E. L. Hirst, *J.*, 1931, 258.

³² Private communication from Professor Hirst.

³³ *J.*, 1939, 558.

the same aldobionic acid, 2- β -glucuronosido-mannose. The chief constituent of cherry gum is, however, *l*-arabofuranose (6 mols.), and in addition the presence has been shown of *d*-galactose (2 mols.), *d*-mannose (1 mol.), *d*-glucuronic acid (1 mol.), and a small proportion (*ca.* 1.5%) of *d*-xylose. This gum appears not to be identical with that from the wild cherry tree. The latter consists of *l*-arabinose (8 mols.), *d*-xylose (6 mols.), *d*-galactose (6 mols.), *d*-mannose (3 mols.), and *d*-glucuronic acid (2 mols.).³⁴

Mucilaginous polysaccharides are extractable from many plants and some of these are extensively used in pharmacy. The few which have been submitted to chemical investigation appear to bear a relationship to pectins on the one hand and to the plant gums on the other. Like the gums, the mucilages appear to possess complex branched-chain structures composed of a number of different monosaccharide units, including a uronic acid. The latter, however, is not glucuronic acid. It is *d*-galacturonic acid, the building unit of pectic acid. The galacturonic acid may usually be isolated in the form of a stable aldobionic acid when the mucilage is submitted to partial hydrolysis. Thus, the well-known slippery elm mucilage yields an aldobionic acid which was shown by E. Anderson³⁵ to be composed of *d*-galacturonic acid and *l*-rhamnose. Later, R. E. Gill, E. L. Hirst, and J. K. N. Jones³⁶ proved that the glycosidic linkage was of the 1 : 2 type found in yeast mannan and damson and cherry gums, and that the aldobionic acid of slippery elm mucilage is correctly described as 2-*d*-galacturonosido-*l*-rhamnose. It is identical with an aldobionic acid obtained from the mucilage of flax seed by R. S. Tipson, C. C. Christman, and P. A. Levene.³⁷ The mucilaginous polysaccharide of the seeds of rib-grass (*Plantago lanceolata*) has been examined by J. Mullan and E. G. V. Percival.³⁸ From this mucilage also there is obtained an aldobionic acid which appears to consist of *d*-galacturonic acid in combination with a methylpentose. The chief constituent of the mucilage is, however, *d*-xylose, and in this preliminary survey, the authors draw attention to the following points: (1) There is an abnormally high proportion of terminal groups of xylopyranose units, an indication of a branched-chain structure. (2) The isolation of 3 : 4-dimethyl xylose among the products of hydrolysis of the methylated mucilage indicates the presence of 1 : 2-glycosidic links involving C₂ of the xylose (cf. the arabans described above). (3) Galactopyranose units are present, although the proportion of galactose is not high. These units are linked by 1 : 3-glycosidic linkages. (4) The nature of the methylpentose is to be the subject of further study.

Arabinose appears to be absent from this mucilage, and in this respect it differs from the mucilage of the seed of *Plantago psyllium*, isolated by E. Anderson and M. Fireman.³⁹ The latter mucilage contains arabinose in addition to xylose and galacturonic acid, but neither galactose nor a methylpentose has been detected in it. The same combination of *l*-arabinose, *d*-galacturonic acid and *d*-xylose is found in the mucilage from Indian

³⁴ C. L. Butler and L. H. Cretcher, *J. Amer. Chem. Soc.*, 1931, **53**, 4161.

³⁵ *J. Biol. Chem.*, 1933, **104**, 163.

³⁶ *J.*, 1939, 1469.

³⁷ *J. Biol. Chem.*, 1939, **128**, 609.

³⁸ *J.*, 1940, 1501.

³⁹ *J. Biol. Chem.*, 1935, **109**, 437.

wheat (*Plantago fastigiata*),⁴⁰ and in a water-soluble polysaccharide from a seaweed, *Enteromorpha compressa*, there are found *l*-arabinose, *l*-rhamnose and a uronic acid.⁴¹ The mucilages of the seeds of white mustard,⁴² quince,⁴³ and cress⁴⁴ appear to be similarly constituted and are distinguished from most other mucilages in that glucose is one of the products of their hydrolysis. It is shown, however, that this sugar arises not from the mucilage proper but from a dispersed cellulose component. Linseed mucilage is of exceptional interest in that it has been shown by E. Anderson⁴⁵ to contain the *l*-form of galactose. This was probably the first demonstration of the presence of *l*-galactose in a natural product and it is to be noted that it is in this case associated with *d*-galacturonic acid.

A polysaccharide extractable by aqueous alcohol from the grain of wheat is worthy of mention in this context because it resembles the gums and mucilages in a structural sense, being composed of more than one type of monosaccharide unit arranged in a branched-chain pattern. But the polysaccharide contains no uronic acid residues and is not acidic. It has often been claimed that the amylolytic enzymes extracted by aqueous alcohol from the grains of wheat, oats, or barley are carbohydrate in nature. An investigation of the β -amylase of wheat by L. H. Ford and S. Peat⁴⁶ demonstrates, however, that the functional part of the amylase is protein in character, but that the protein is always associated with a soluble polysaccharide. It was possible by chemical means to separate the polysaccharide from the other constituents of the enzyme complex, and it was then shown to have no amylolytic activity. The real function of the polysaccharide remains to be determined, but in the meantime its chemical constitution has been investigated. It is composed entirely of *l*-arabinose, *d*-xylose and *d*-galactose, and, as already stated, it contains no acidic residues.

The methylated polysaccharide is easily resolved by hydrolysis into its constituent monosaccharides, which were shown to be trimethyl *l*-arabofuranose (6 mols.), 2 : 3-dimethyl xylose (6 mols.), 2-methyl xylose (1 mol.), xylose (1 mol.) and 2 : 4-dimethyl galactose (1 mol.).

From this analysis it is evident that the polysaccharide is of the complex branched-chain type, the terminal units of which are constituted by *l*-arabinose existing (as in the arabans, gums and mucilages) entirely in the furanose form.

The main chain of the repeating unit is obviously composed chiefly of *d*-xylose residues and although it cannot be determined at present whether these residues are pyranose or furanose, it is probable that in this polysaccharide, as in all other xylans investigated, the xylose is pyranose. It follows that the linkages involving the xylose are mainly 1 : 4-glycosidic

⁴⁰ E. Anderson, L. A. Gillette, and M. G. Seeley, *J. Biol. Chem.*, 1941, **140**, 569.

⁴¹ S. Miyake and K. Hayasi, *Chem. Abstr.*, 1940, 6933.

⁴² K. Bailey and F. W. Norris, *Biochem. J.*, 1932, **26**, 1609.

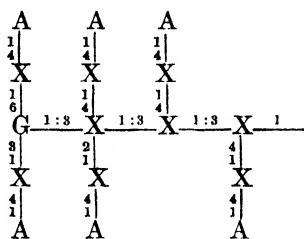
⁴³ A. G. Renfrew and L. H. Cretcher, *J. Biol. Chem.*, 1932, **97**, 503.

⁴⁴ K. Bailey, *Biochem. J.*, 1935, **29**, 2477.

⁴⁵ *J. Biol. Chem.*, 1933, **100**, 249.

⁴⁶ *J.*, 1941, 856.

and xylose residues so linked are interposed between the terminal *l*-arabofuranose members and the main chain. It is seen that the familiar 2:4-dimethyl galactose of the methylated gums and mucilages appears also in this methylated polysaccharide, although its proportion is small. It implies the presence in the polysaccharide repeating unit of one *d*-galactopyranose residue which is combined with other members through positions 1, 3 and 6, and must therefore constitute part of the main chain. One of the many ways in which these facts may be correlated and represented pictorially is shown in (XIX).

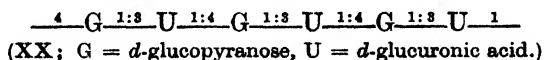


(XIX; A = *l*-arabofuranose, X = *d*-xylopyranose, G = *d*-galactopyranose.)

It is thus seen to be essentially a xyloaraban in which the pentose units are mutually combined by 1:2-, 1:3- and 1:4-glycosidic linkages with the last two predominating. In addition, it contains a galactose residue which is attached at three points to other residues.

Two other recently investigated polysaccharides of this type remain to be mentioned. The chemical investigation of the highly significant capsular polysaccharides of pneumococci has been carried one step further by R. E. Reeves and W. F. Goebel.⁴⁷ It had earlier been shown that the repeating unit of the polysaccharide of pneumococcus type III was cellobiuronic acid, *i.e.*, 4- β -glucuronosidoglucose, and now the nature of the glycosidic linkages between these aldobionic acid units has been elucidated by the methylation method.

It has already been indicated that the glucuronosido-linkage in aldobionic acids is resistant to hydrolytic agents and for that reason, Reeves and Goebel submitted the methylated polysaccharide ester to reduction with hydrogen at 175° under pressure and in the presence of a barium-copper chromite catalyst. By this procedure the carbomethoxy-group of the methylated glucuronic ester residue was reduced to a primary alcohol group. As a result, the methylated polysaccharide now consisted of a chain of methylated glucose residues only, and hydrolysis with acid was easily effected. There was isolated from the hydrolysate, in addition to 2:3:6-trimethyl glucose (from the original glucose constituents of the polysaccharide), a dimethyl glucose (from the original glucuronic acid constituent) which was proved to be 2:4-dimethyl glucose. Clearly the linkage between two units of cellobiuronic acid engages C₃ of the uronic acid and the polysaccharide may now be represented by (XX).



⁴⁷ *J. Biol. Chem.*, 1941, **139**, 511.

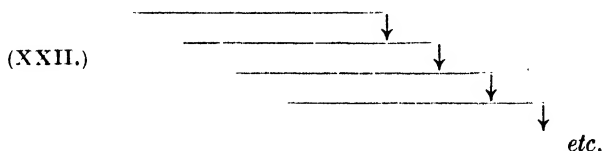
⁴⁸ *J.*, 1940, 184; *idem*, unpublished.

solution of the methyl derivative is very small; and the carbohydrate shows no reducing power.

Starch.

Recent developments in the chemistry of starch have taken place along three main lines: (1) The synthesis of the polysaccharide *in vitro*; (2) the probable chemical heterogeneity of whole starch and (3) its branching chain structure.

There has been a recrudescence of interest in the finer points of the structure of starch, particularly in regard to the mode of branching of the basal chains. The branched-chain structure of starch has been put forward in some quarters as a new idea, but it should be remembered that the idea is implicit in the Haworth-Hirst conception of the constitution of starch and of other polysaccharides and was indeed stated in precise terms as long ago as 1934.⁴⁹ The method of end-group assay which was developed originally in connection with the chain-length of cellulose has been applied to whole starches from many natural sources, and in every case approximately the same proportion of end-group has been found. Recent examples are furnished by the assay of rice starch,⁵⁰ banana starch,⁵¹ wheat starch and horse-chestnut starch.⁵² This proportion indicates the presence of one non-reducing terminal group in 24–30 glucose residues. This chain of 24–30 glucose members obviously does not constitute the whole molecule of starch, but is in fact a repeating unit and starch consists of aggregates of these repeating units. There was at first insufficient evidence to allow of a definite conclusion in regard to the precise nature of the linkage between repeating units, but that starch consisted of ramified chains was self-evident and the conception was given pictorial expression by Haworth and Hirst in the laminated formulation (XXII).



In the diagram, the horizontal lines represent the unit chains of monosaccharide units (24–30 glucose residues in the case of natural starch) and the arrow heads indicate the linking of the reducing terminal units of the chains. The linkage between the repeating units is referred to for convenience as a polymeric bond.⁵³

The nature of the polymeric link was left unspecified in 1934, but it was subsequently shown by C. E. H. Bawn, E. L. Hirst, and G. T. Young⁵⁴

⁴⁹ W. N. Haworth, E. L. Hirst, and E. Oliver, *J.*, 1934, 1917.

⁵⁰ E. L. Hirst and G. T. Young, *J.*, 1939, 1471.

⁵¹ E. G. E. Hawkins, J. K. N. Jones and, G. T. Young, *J.*, 1940, 390.

⁵² E. L. Hirst and G. T. Young, *J.*, 1939, 951.

⁵³ W. N. Haworth, *Chem. and Ind.*, 1939, 58, 917.

⁵⁴ *Trans. Faraday Soc.*, 1940, 36, 880.

that these linkages are made by primary valencies. Furthermore, evidence was adduced to show that the linkages between repeating units were α -1:6-glycosidic, as was first portrayed by W. N. Haworth, E. L. Hirst, and F. A. Isherwood.⁵⁵ This evidence was provided by C. C. Barker, E. L. Hirst, and G. T. Young,⁵⁶ and by K. Freudenberg and H. Boppel⁵⁷ from an examination of the dimethyl glucose fraction of the hydrolysate of a highly methylated starch. This fraction consisted chiefly of 2:3-dimethyl glucose, which was present in an amount equivalent to that of the end-group, tetramethyl glucose. K. Myrbäck, from a consideration of the specific rotations of some limit dextrins, expressed the view that there were present a small number of α -1:6-glycosidic linkings⁵⁸ and K. H. Meyer and P. Bernfeld demonstrated that the polymeric bonds were α -glycosidic, inasmuch as they underwent fission with an α -glucosidase but not with β -amylase.⁵⁹

There are thus two types of linkage in starch. The glucose members of the repeating unit are combined by α -1:4-glucosidic linkages (maltose linkages) and the repeating units themselves are joined by α -1:6-glucosidic links (the so-called isomaltose link).

The method of assay in which the proportion of non-reducing terminal groups is estimated has been supplemented by the mercaptalation method of M. L. Wolfrom. This method consists in the hydrolysis of methylated starch with concentrated hydrochloric acid in the presence of ethyl mercaptan. The latter reacts with the reducing groups as they are released by hydrolysis. Samples are removed during the course of the hydrolysis and the amount of sulphur which has entered into combination is estimated. By extrapolation, the proportion of reducing group originally present is calculated. It is thus a dynamic end-group assay and is not limited to an end-group originally present. Moreover, it is to be observed that by this method it is the reducing terminal group that is estimated and the assay is therefore independent of branching. It was shown that the average degree of polymerisation varied from 34 glucose residues at 1½ hours to 3 after 21 hours. Extrapolation showed an initial average degree of polymerisation not greater than 150 glucose units.⁶⁰ It is concluded that the repeating unit of 24—30 glucose residues does not represent the whole molecule of native starch, a conclusion that is of course in keeping with the current hypothesis.

Although a branched-chain structure of the type discussed represents the constitution of the chief component of starch, it is becoming increasingly evident that a component differently constituted is also present. It will be appropriate in this connection to refer first to the synthetic starch of C. S. Hanes. This is produced *in vitro* from glucose 1-phosphate by the agency of a phosphorylase which is extractable from many plants, including the potato.⁶¹ The synthetic starch closely resembles native potato starch but

⁵⁵ *J.*, 1937, 577.

⁵⁶ *Nature*, 1941, 147, 296.

⁵⁷ *Chem. Abstr.*, 1941, 35, 439.

⁵⁸ *Svensk Kem. Tidskr.*, 1940, 52, 126.

⁵⁹ *Helv. Chim. Acta*, 1940, 23, 875.

⁶⁰ M. L. Wolfrom and D. R. Myers, *J. Amer. Chem. Soc.*, 1941, 63, 1336.

⁶¹ *Proc. Roy. Soc.*, 1940, B, 128, 421; 129, 174.

differs from it in at least one notable particular. The synthetic starch is completely converted into maltose by β -amylase, whereas the hydrolysis of natural starch by this enzyme ceases when 60% conversion has been effected. Another significant difference came to light when a sample of synthetic starch prepared by Dr. Hanes was assayed by the end-group method by W. N. Haworth, R. L. Heath, and S. Peat.⁶² The starch was thus shown to be constituted of chains of glucose members united by the usual α -1 : 4-glycosidic linkages, but the proportion of terminal groups was much smaller than in the case of whole potato starch and corresponded to an apparent chain length of not less than 80—90 glucose members. It has not yet been possible to determine the particle size of synthetic starch by the osmotic pressure method, but determination of the viscosities of solutions of the methylated starch (the Staudinger constant for linear polymers such as cellulose being used) indicates an average molecular size of 80—160 glucose residues. There is thus some probability that synthetic starch is not a highly branched structure like native starch, and may even consist of single chains of approximately 100 glucose members. W. Z. Hassid and R. M. McCready,⁶³ who have also methylated and hydrolysed a synthetic starch prepared by Hanes's method, have failed to detect any tetramethyl glucose end-group at all. It is pointed out, however, that the quantity of methylated starch employed for the determination by these authors may have been insufficient to ensure the assay of the small amount of end-group (a maximum of 1.5%) found by Haworth, Heath, and Peat.

A question of great interest arises. Is this long-chain variety of starch solely a product of laboratory synthesis, or is it present also in natural starch? It is well known that native starch is separable by a number of physical processes into two main components which are distinguished by differences of physical properties. Such components have been variously called amylopectin and amylose, α - and β -amylose, amyloamylose and erythroamylose. There have been some grounds for the view that these two components are constituted of the same fundamental repeating unit and differ only in the degree of aggregation or polymerisation of this repeating unit. However, the possibility of the existence of a chemical difference between the two has never been excluded, and certain recently discovered facts reopen the question. Thus it is reported by M. Samec and E. Waldschmidt-Leitz,⁶⁴ and confirmed by G. Freeman and R. H. Hopkins,⁶⁵ that amyloamylose (which is prepared by a process involving the dispersion of potato starch in water by autoclaving at 120° and the submission of the solution to electro-dialysis) is completely hydrolysed by β -amylase. In this property it is identical with synthetic starch.

The end-group assay was subsequently applied to amyloamylose and erythroamylose (*i.e.*, the two starch components separated by electrophoresis) by K. Hess and B. Krajnc,⁶⁶ who found the degrees of polymeris-

⁶² *J.*, 1942, 55.

⁶³ *Z. physiol. Chem.*, 1931, 203, 16.

⁶⁶ *Chem. Abstr.*, 1941, 35, 3612.

⁶³ *J. Amer. Chem. Soc.*, 1941, 63, 2171.

⁶⁵ *Biochem. J.*, 1936, 30, 446.

ation of the two substances to be 283 and 23 glucose members respectively. Further evidence of the chemical heterogeneity of starch came from K. H. Meyer,⁶⁷ who separated an amylose (5%) from the intact grain of maize or potato starch by extraction with water at 60–70°. The undissolved residue is referred to as amylopectin. Rough end-group estimations showed that, whereas the amylopectin was constituted of short-chain (24–30 glucose residues) repeating units, the chain-length of the amylose was of the order of 300 glucose units. Furthermore, the molecular weight of methylated amylose determined by osmotic pressure measurement was of the same order, an indication that the chain unit of amylose is not branched. K. Hess and E. Steurer⁶⁸ agree that starch contains a long-chain component (20–25% of the whole) but find that the degree of polymerisation of this component when methylated is 240 by end-group assay and 650 by osmotic pressure measurement. Some branching is therefore indicated, approximately 3 repeating units being linked together.

To the amylopectin (or erythroamylose) component is assigned the highly ramified or laminated structure (XXII), and this constitutes about 80% of the whole starch. K. H. Meyer⁶⁹ has attempted a more precise representation of the structure of amylopectin than that given by (XXII), a representation which envisages multiple branching rather than the single branching of (XXII), although the principle of the two types of aggregation is the same. Meyer bases his view on a consideration of the course of amyolytic breakdown of amylopectin and of the limit dextrins produced during that degradation, but, in the opinion of the Reporter, a sufficient body of fact is not yet available to justify a more precise portrayal of the constitution of amylopectin than that given by the Haworth–Hirst model. An ingenious attempt to define with arithmetical exactitude the constitution of amylopectin and to explain the sequence of changes leading to the product of limit dextrins has been made by C. O. Bechmann and J. C. Coles.⁷⁰

In conclusion, the attention of the reader is drawn to a comprehensive investigation by L. H. Lampitt, C. H. F. Fuller, and N. Goldenberg⁷¹ of the effect of dry grinding upon the physical properties and molecular size of wheat starch.

S. P.

5. SYNTHETIC POLYENES.

Interest in compounds containing a multiplicity of conjugated ethylenic linkages has centred around either the correlation of physical and chemical properties with constitution or attempts to synthesise vitamin A, carotenoids or related substances. Such studies, more especially with the aliphatic polyenes, are fraught with difficulty in that these substances are character-

⁶⁷ K. H. Meyer, M. Wertheim, and P. Bernfeld, *Helv. Chim. Acta*, 1940, **23**, 865; 1941, **24**, 378.

⁶⁸ *Chem. Abstr.*, 1941, **35**, 4743.

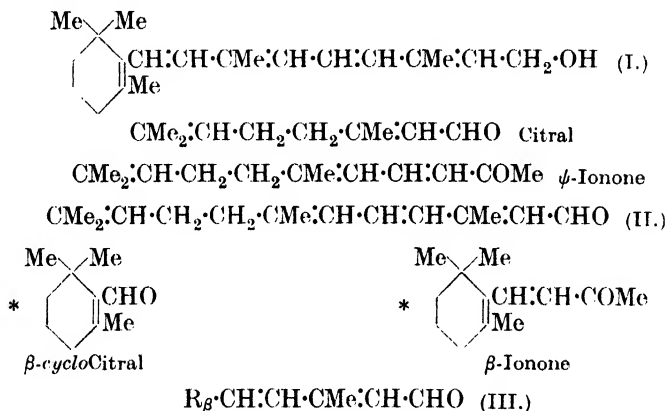
⁶⁹ K. H. Meyer and P. Bernfeld, *Helv. Chim. Acta*, 1940, **23**, 875.

⁷⁰ *Chem. and Ind.*, 1941, **60**, 750.

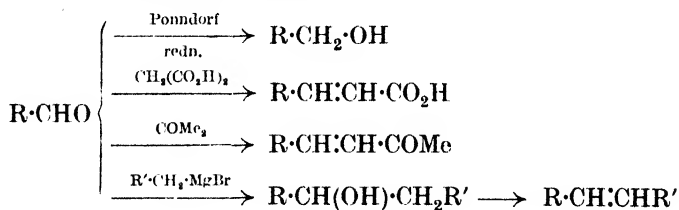
⁷¹ *J. Soc. Chem. Ind.*, 1941, **60**, 1, 25, 47, 69, 99, 137.

ised by an extreme lability towards oxygen and, frequently, mineral acids. Distillation of the higher members even at very low pressures is usually impossible owing to decomposition, the simultaneous production of geometrical isomerides tends to inhibit crystallisation, and consequently the main criterion of purity is the absorption spectrum, the most characteristic property of the conjugated polyenes, and facilities for its determination are not readily available. No comprehensive account of the work in this field has appeared hitherto in these Reports, but a survey of the fundamental work of the Heidelberg school was made by R. Kuhn¹ in a Pedler lecture and a general account of synthetic work in the polyene series has been written by M. T. Bogert.²

The citrals and ionones are obvious starting materials for vitamin A (I) or carotenoid syntheses; the corresponding C_{15} -aldehydes (ψ - and β -ionylideneacetaldehydes, II and III) and the C_{18} -ketones derivable from them by condensation with acetone are important intermediates, some of which have now been synthesised.



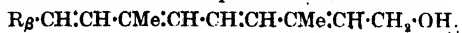
Many studies of the preparation and reactions of the polyene aldehydes have been made and their importance in this field is clearly illustrated by the following well-known conversions :



¹ J., 1938, 605.

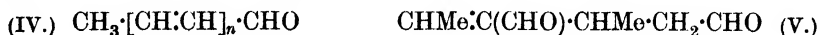
² H. Gilman's "Organic Chemistry." Wiley, New York; Chapman and Hall, London, 1938.

* The β -ionone ring (2:2:6-trimethyl- Δ^4 -cyclohexenyl-) will subsequently be designated $\text{R}\beta$, e.g., vitamin A would be represented as



Condensations with Acetaldehyde and Crotonaldehyde.

Indifferent yields of impure products had been obtained by early workers,³ employing either zinc chloride or sodium acetate as catalyst for the self-condensation of acetaldehyde. In 1930, however, R. Kuhn and M. Hoffer⁴ discovered that secondary amines, long known to be useful catalysts in the Knoevenagel reaction,⁵ were equally effective in bringing about condensation of acetaldehyde either with itself or with crotonaldehyde; they prepared sorbaldehyde (hexadienal, IV; $n = 2$) and octatrienal (IV; $n = 3$)



by means of piperidine. Improvements in this condensation, resulting in the isolation in addition of decatetraenal (IV; $n = 4$), have been described by other workers^{6, 7, 8} and the catalytic effect of monoamino-acids, most marked at p_H 7—8, has been observed.⁹

Crotonaldehyde yields the expected aldol in presence of potassium carbonate,¹⁰ but was reported not to condense in the presence of piperidine.⁴ Bernhauer and his collaborators,^{11, 12, 13, 14} however, employing this base as catalyst, described the formation of the linear condensation product, octatrienal (IV; $n = 3$), together with dihydro-*o*-tolualdehyde and dicrotonaldehyde (V), the products being identified in general by fractional distillation and oxidation of the fractions with silver oxide to octatrienic acid, dihydro-*o*-toluic acid and dicrotonic acid respectively. Small amounts of *p*-toluic acid were also isolated from the oxidation product, the corresponding aldehyde and 1 : 2-dihydro-*o*-tolualdehyde, probably being derived from an intermediate aldol (VI) by cyclisations in the 2 : 7- and 1 : 6-positions respectively, and the aldehyde (V) would appear to be formed by a type of Michael condensation. R. Kuhn, W. Badstübner, and C. Grundmann⁸ explained the negative result of Kuhn and Hoffer⁴ by the observation that, whereas pure crotonaldehyde is unaffected by piperidine, the impure aldehyde, containing crotonic acid, self-condenses readily, and demonstrated that a piperidine salt rather than the free base is the effective catalyst.

³ A. Kekulé, *Annalen*, 1872, **162**, 77; S. Ziesel and B. von Bitto, *Monatsh.*, 1908, **29**, 591; S. Ziesel and M. Neuwirth, *Annalen*, 1923, **433**, 121.

⁴ *Ber.*, 1930, **63**, 2164; 1931, **64**, 1977.

⁵ E. Knoevenagel, *Annalen*, 1894, **281**, 25; *Ber.*, 1904, **37**, 4461.

⁶ T. Reichstein, C. Ammann, and G. Trivelli, *Helv. Chim. Acta*, 1932, **15**, 261; T. Reichstein and G. Trivelli, *ibid.*, 1932, **15**, 1074.

⁷ F. G. Fischer and O. Wiedemann, *Annalen*, 1934, **513**, 251.

⁸ R. Kuhn, W. Badstübner, and C. Grundmann, *Ber.*, 1936, **69**, 98.

⁹ F. G. Fischer and A. Marschall, *Ber.*, 1931, **64**, 2825.

¹⁰ I. Smedley, *J.*, 1911, **99**, 1627.

¹¹ K. Bernhauer and E. Woldan, *Biochem. Z.*, 1932, **249**, 199.

¹² K. Bernhauer and E. Neubauer, *ibid.*, 1932, **251**, 173; K. Bernhauer and K. Irrgang, *ibid.*, 1932, **254**, 434.

¹³ K. Bernhauer and R. Drobnick, *ibid.*, 1933, **266**, 197.

¹⁴ K. Bernhauer and K. Irrgang, *Annalen*, 1936, **525**, 43.

F. G. Fischer, K. Hultsch, and W. Flaig¹⁵ claim that these aldehyde condensations are better catalysed by a solution of piperidine in excess of acetic acid, obtaining from crotonaldehyde, dihydro-*o*-tolualdehyde and other cyclic condensation products, octatrienal (15% yield) and dodecapentaenal (IV; $n = 5$) in 4% yield. The latter aldehyde has also been prepared in similar yield by use of the neutral piperidine acetate catalyst.^{16, 17} The highest member of the series of crotonaldehyde self-condensation products to be isolated in a pure condition is the red hexadecaheptaenal (IV; $n = 7$).^{17, 18} Various catalysts for these condensations have been examined; ^{14, 15, 19} piperidine acetate and salts of similar secondary bases, such as morpholine and piperazine, are apparently the most effective. The concentration and also the purity of the catalyst are important factors, the constitution of the solvent has a marked effect on reaction velocity ^{14, 19, 20} and in alcoholic solution, alkoxy-polyene aldehydes are formed.¹⁹ This addition of solvent can be eliminated by using 70% alcohol.¹⁷

It has been found that condensation between crotonaldehyde and the higher polyene aldehydes proceeds smoothly, a 12.5% yield of dodecapentaenal being achieved from octatrienal with piperidine acetate.¹⁶ Quite recently J. Schmidt¹⁷ has studied these condensations in detail, employing a considerable excess of the lower aldehyde in a solvent and much greater quantities of the neutral piperidine acetate catalyst than have generally been used by previous workers. Condensation of crotonaldehyde with sorbaldehyde in 70% alcohol gave the new tetradecaheptaenal (IV; $n = 6$) and some impure octadecaheptaenal (IV; $n = 8$), and from octatrienal with crotonaldehyde in benzene a 20% yield of dodecapentaenal was obtained.

No definite conclusions as to the mechanism of catalysis of aldehyde condensations by the salts of secondary bases can as yet be drawn,²¹ but a recent observation by W. Langenbeck and O. Gödde²² is of interest. 1-Piperidylbutadiene, formed when crotonaldehyde reacts with piperidine salts, condenses readily with acetaldehyde and on decomposition with acetic anhydride-acetic acid the product yields sorbaldehyde and piperidine. Similar decomposition of the crotonaldehyde-piperidylbutadiene product gives dihydro-*o*-tolualdehyde, but if condensation is carried out in the presence of acetic acid, octatrienal is formed.

Self-condensation of Methylcrotonaldehyde.

β -Methylcrotonaldehyde (VII), possessing the carbon skeleton of isoprene, offers distinct promise as a starting material for the synthesis of substances of the carotenoid or vitamin A type. It was first prepared from isovaler-

¹⁵ *Ber.*, 1937, **70**, 370.

¹⁶ R. Kuhn and C. Grundmann, *Ber.*, 1937, **70**, 1318.

¹⁷ *Annalen*, 1941, **547**, 285.

¹⁸ R. Kuhn, C. Grundmann, and H. Trischmann, *Z. physiol. Chem.*, 1937, **248**, IV.

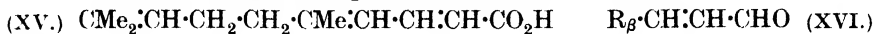
¹⁹ R. Kuhn and C. Grundmann, *Ber.*, 1938, **71**, 2274.

²⁰ H. L. du Mont and H. Fleischhauer, *Ber.*, 1938, **71**, 1958.

²¹ See *Ann. Reports*, 1939, **36**, 210.

²² *Chem. Abstr.*, 1940, **34**, 1970.

more complex intermediates for vitamin A synthesis could be made in this way from their acyclic analogues, *e.g.*, β -ionylideneacetaldehyde (III) by cyclisation of ψ -ionylideneacetaldehyde (II).^{11, 33} Consequently some attention has been devoted to the preparation of acyclic polyene aldehydes from citral, compounds which could also be employed for a lycopene or γ -carotene synthesis. Condensation of acetaldehyde with citral in the presence of piperidine acetate^{8, 33} or sodamide³⁴ gives citrylideneacetaldehyde (XIV) in 30% yield. It is readily characterised by crystalline derivatives (semicarbazone, m. p. 166—167°) and its absorption spectrum, and its consti-



tution has been rigidly proved.⁸ Further confirmation of this was provided by the preparation of (XIV) by distillation of the barium salt of citrylideneacetic acid (XV) with barium formate.³³ On the other hand, reduction of the phenylimidochloride of (XV) with chromous chloride in ether³⁵ gave a mixture of aldehydes from which two semicarbazones, both different from that described above, were prepared and it has been suggested³⁶ that *cis-trans* isomerism is responsible for this discrepancy (see, however, ref. 8). Cyclisation of the semicarbazone of (XIV) with phosphoric acid³⁷ yields β -cyclocitrylideneacetaldehyde (XVI), giving geronic acid ($\text{CO}_2\text{H}\cdot\text{CMe}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COMe}$) on ozonolysis, the presence of the β -ionone ring thus being proved.

The condensation of citral with both crotonaldehyde and β -methylcrotonaldehyde has been investigated with considerable success by I. M. Heilbron and his co-workers,^{33, 34} resulting in the preparation of a number of well-characterised C_{14} and C_{15} aldehydes. It is impossible to deal in detail here with the determination of the constitution of the individual aldehydes, but in general the evidence consists of light absorption data for the aldehydes, their semicarbazones and the corresponding alcohols, and ozonolysis experiments and quantitative microhydrogenation of the semicarbazones (the semicarbazido-linkage takes up 2H) and alcohols. From citral and crotonaldehyde, with either neutral or acid piperidine acetate (improved by the addition of silica gel), citrylideneacetaldehydes-*a* and -*b* (XVIIa and XVIIb), readily separated as the semicarbazones, and a third cyclic C_{14} aldehyde have been isolated. Additional evidence for the constitution of (XVIIa) is furnished by its isolation along with citrylideneacetaldehyde (XIV) from the condensation product of citral and acetaldehyde (piperidine acetate). Yet another cyclic C_{14} aldehyde is produced, together with (XVIIa), by the sodamide-catalysed interaction of citral and crotonaldehyde, or accompanying (XIV) by a similar interaction

³³ J. W. Batty, A. Burawoy, I. M. Heilbron, W. E. Jones, and A. Lowe, *J.*, 1937, 755.

³⁴ E. Barraclough, J. W. Batty, I. M. Heilbron, and W. E. Jones, *J.*, 1939, 1549.

³⁵ J. von Braun and W. Rudolph, *Ber.*, 1934, **67**, 269, 1735.

³⁶ J. von Braun and P. Kurtz, *Ber.*, 1937, **70**, 1009.

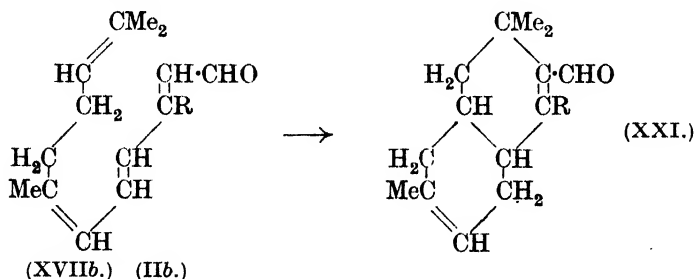
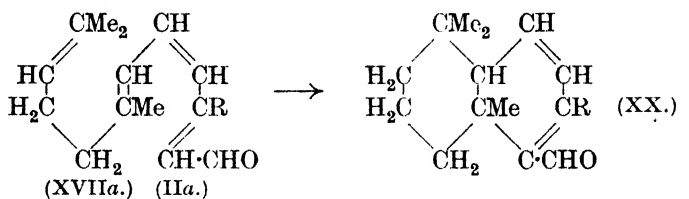
³⁷ I. M. Heilbron, W. E. Jones, and A. Spinks, *J.*, 1939, 1554.

of citral and acetaldehyde. It is noteworthy that acyclic aldehydes are produced in these sodamide condensations, since β -methylcrotonaldehyde itself gives essentially cyclic products under these conditions.²⁴

Condensation of citral with β -methylcrotonaldehyde in the presence of neutral or acid piperidine acetate gives unsatisfactory results, but with sodamide in ethereal solution smooth condensation occurs, yielding ψ -ionylideneacetaldehydes-*a* and -*b* (IIa and IIb), also readily separated as the semicarbazones. Both (XVIIa) and (IIa), the major products from the respective condensations, react with acetone in the presence of sodium ethoxide, yielding the penta-ethenoid C_{17} and C_{18} ketones (XVIII) and (XIX).



The semicarbazones of the four acyclic ketones described above were treated with cold phosphoric acid³⁸ in an endeavour to obtain monocyclic C_{14} and C_{15} aldehydes, such as β -ionylideneacetaldehyde (III). Smooth cyclisation takes place under these conditions, yielding, however, bicyclic aldehydes which are unfortunately of little synthetic value. The acyclic (XVIIa) and (IIa) are cyclised to the aldehydes (XX; $R = H$ and Me respectively) with two double bonds in conjugation with the aldehyde group, and (XVIIb) and (IIb) yield the $\alpha\beta$ -unsaturated aldehydes (XXI; $R = H$ and Me respectively).



During a study of the action of the Oppenauer reagent (aluminium *tert.*-butoxide and acetone) on vitamin A, it was discovered³⁹ that a C_{23} ketone was readily formed and it was then ascertained that the method is one which can be applied generally to $\beta\gamma$ -unsaturated primary alcohols,

³⁸ J. W. Batty, I. M. Heilbron, and W. E. Jones, *J.*, 1939, 1556.

³⁹ J. W. Batty, A. Burawoy, S. H. Harper, I. M. Heilbron, and W. E. Jones, *J.*, 1938, 175.

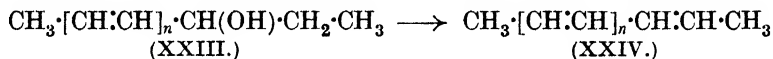
$R\cdot CH:CH\cdot CH_2\cdot OH$, to effect conversion into the higher ketones, $R\cdot CH:CH\cdot CH:CH\cdot COMe$. The importance of this reaction from the vitamin A synthesis aspect lies in the fact that, given a suitable method of converting β -ionone into the C_{15} alcohol (XXII), the modified Oppenauer reaction would yield the C_{18} ketone, on which the alcohol synthesis could



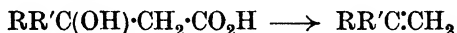
be repeated to give vitamin A. In subsequent publications^{40, 41} it has been shown that with diethyl or, better, diisopropyl ketone as hydrogen acceptor, the Oppenauer reaction can be made to yield unsaturated aldehydes, although in rather poor yield.

Aliphatic Polyene Hydrocarbons.

Comparatively few studies of the higher aliphatic polyene hydrocarbons have been made. R. Kuhn and C. Grundmann,⁴² by the reaction of sorb-aldehyde (IV; $n = 2$), octatrienal (IV; $n = 3$), and dodecapentaenal (IV; $n = 5$) with ethylmagnesium bromide, obtained the secondary carbinols (XXIII; $n = 2, 3$, and 5) in moderate yields. Dehydration with



p-toluenesulphonic acid in ether or dioxan solution furnished the dimethylpolyenes (XXIV), that derived from dodecapentaenal, namely, 1:12-dimethyldodecahexaene (XXIV; $n = 5$), which forms yellow needles, being the first synthetic coloured aliphatic hydrocarbon to be prepared. Both the hydrocarbons and the carbinols rapidly autoxidise and polymerise. Treatment of allyl chloride and methallyl chloride ($CH_2\cdot CMe\cdot CH_2Cl$) with sodamide in liquid ammonia yields hexatriene and 2:5-dimethylhexatriene respectively⁴³ in about 25% yield. F. G. Fischer and K. Löwenberg⁴⁴ have prepared polyene hydrocarbons by the decarboxylation of unsaturated β -hydroxy-acids, the reaction being facilitated by the accumulation of double bonds in the molecule.



Polyene Alcohols.

The application of the highly specific Ponndorf reduction method (aluminium isopropoxide and isopropyl alcohol)⁴⁵ to polyene aldehydes⁶ provided the first convenient method of preparing these alcohols and opened up the possibility of obtaining vitamin A by reduction of a C_{20} aldehyde.

⁴⁰ E. Haworth, I. M. Heilbron, W. E. Jones, A. L. Morrison, and J. B. Polya, *J.*, 1939, 128.

⁴¹ I. M. Heilbron, A. W. Johnson, and W. E. Jones, *ibid.*, p. 1560.

⁴² *Ber.*, 1938, 71, 442.

⁴³ M. S. Kharasch and E. Sternfeld, *J. Amer. Chem. Soc.*, 1939, 61, 2318; M. S. Kharasch, W. Nudenberg, and E. Sternfeld, *ibid.*, 1940, 62, 2034.

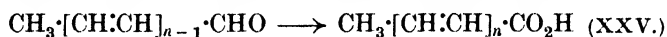
⁴⁴ *Ber.*, 1933, 66, 669.

⁴⁵ *Ann. Reports*, 1937, 34, 228; T. Bersin, *Angew. Chem.*, 1940, 53, 266.

From the corresponding aldehydes, hexadienol, octatrienol and decatetraenol were all obtained in good yields as crystalline solids and many other polyene alcohols have been made available by this means (dehydrogeraniol and farnesinol;²⁹ dodecapentaenol;¹⁵ citrylidene-ethyl alcohol;⁸ 11-phenylundecapentaenol;⁴⁶ C₁₄ and C₁₅ alcohols³⁴). Both farnesinol and dodecapentaenol, which are closely analogous to vitamin A in chromophoric structure, give the same deep blue antimony trichloride coloration as the vitamin.

Polyene Carboxylic Acids.

The simpler members of this series are more or less readily prepared by oxidation of the appropriate aldehyde with silver oxide,^{6, 14, 29, 47} but the extension of Doebner's synthesis⁴⁸ of sorbic acid (XXV; $n = 2$) from crotonaldehyde and malonic acid in the presence of pyridine has provided the most general method for the synthesis of polyene carboxylic acids. In



this way R. Kuhn and M. Hoffer⁴ obtained octatrienic and decatetraenic acids (XXV; $n = 3$ and 4) from hexadienal (IV; $n = 2$) and octatrienal (IV; $n = 3$) respectively. The simpler malonic acids are decarboxylated during the condensation, but the higher acids are decarboxylated conveniently either in boiling acetic anhydride⁴⁹ or in boiling acetic acid-acetic anhydride.⁸ The higher polyene aldehydes condense with malonic acid in good yield only in the presence of piperidine,¹⁶ but with the lower aldehydes piperidine addition has a deleterious effect, since it readily catalyses the self-condensation of the aldehydes. A direct synthesis of stearic acid has been achieved by hydrogenation and decarboxylation of the malonic acid from hexadecaheptaenal (IV; $n = 7$),¹⁸ and a similar synthesis from tetradecahexaenal (IV; $n = 6$) yielded palmitic acid.¹⁷ 7-Phenylheptatrienic acid (XXVI; $n = 3$)⁴⁹ and 13-phenyltridecahexaenic acid (XXVI; $n = 6$)⁴⁶ have been synthesised from the appropriate phenyl polyene aldehydes by Doebner's method.



The Reformatsky reaction has been applied to a limited extent in this field, notably to the synthesis of dehydrogeranic acid⁵⁰ and β -ionylideneacetic ester (XXVII).⁵¹ An interesting and potentially useful extension of this reaction is reported by R. C. Fuson, R. T. Arnold, and H. G. Cooke,⁵² who found that γ -iodocrotonic ester (XXVIII) is sufficiently activated to undergo a Reformatsky reaction with aldehydes and ketones. For

⁴⁶ R. Kuhn and K. Wallenfels, *Ber.*, 1937, **70**, 1331.

⁴⁷ A. Kekulé, *Annalen*, 1872, **162**, 77; D. Vorländer, E. Fischer, and K. Kunze, *Ber.*, 1925, **58**, 1984.

⁴⁸ O. Doebner, *Ber.*, 1900, **33**, 2140.

⁴⁹ D. Vorländer and E. Daehn, *Ber.*, 1929, **62**, 545.

⁵⁰ *Ann. Reports*, 1932, **29**, 117.

⁵¹ P. Karrer, H. Salomon, R. Morf, and O. Walker, *Helv. Chim. Acta*, 1932, **15**, 878.

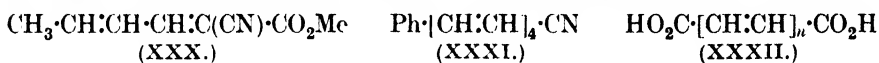
⁵² *J. Amer. Chem. Soc.*, 1938, **60**, 2272.

example, with benzaldehyde, the intermediate hydroxy-ester so obtained is dehydrated on hydrolysis, yielding phenylpentadienic acid (XXVI; $n = 2$).



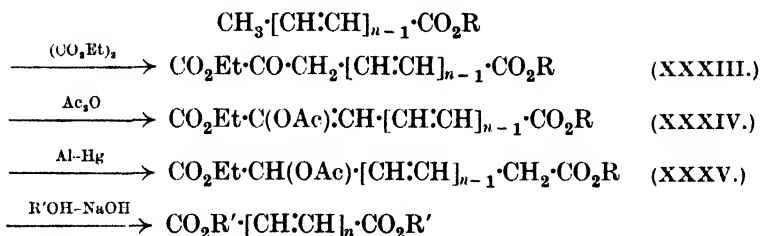
The keto-acid synthesis from cinnamaldehyde and pyruvic acid ⁵³ has been applied by F. G. Fischer and O. Wiedemann ⁵⁴ to the preparation of aliphatic keto-acids of the polyene type (XXIX; $n = 2, 3$, and 4). Condensation between the aldehyde and the pyruvic acid is rapidly carried out under the influence of strong alkali and the yields increase with the molecular weight of the aldehyde, owing to the diminishing tendency of the higher members to self-condensation.

A. C. Cope⁵⁵ observed that excellent yields are obtainable in the Knoevenagel condensation of ketones with methyl cyanoacetate when acetates of bases or acetamide in acetic acid are employed as catalysts and the water formed in the condensation is continuously removed by distillation. This method has been used for the synthesis of a number of unsaturated cyano-esters and nitriles⁵⁶ and it is interesting to note an extension to the condensation of cinnamaldehyde with methyl α -cyanosorbate (XXX), leading eventually to the preparation of phenylnonatetraenonitrile (XXXI).



Polyene Dicarboxylic Acids.

Until recently muconic acid (XXXII; $n = 2$) was the highest known member of the series of symmetrical polyene dicarboxylic acids (XXXII). R. Kuhn and C. Grundmann,^{16, 57, 58, 59} however, have now synthesised several higher members (XXXII; $n = 3, 4, 5$, and 7) from the lower monocarboxylic acids by the procedure outlined below :



Earlier workers had investigated the condensation of ethyl oxalate with crotonic ⁶⁰ and sorbic ⁶¹ esters to the oxalo-esters (XXXIII) and a careful

⁵³ E. Erlenmeyer, *Ber.*, 1903, **36**, 2527; 1904, **37**, 1318; E. Friedmann and H. Mai, *Helv. Chim. Acta*, 1931, **14**, 1213.

⁵⁴ *Annalen*, 1934, 518, 251.

⁵⁵ *J. Amer. Chem. Soc.*, 1937, **59**, 2327.

⁵⁶ G. Wittig and H. Hartmann, *Ber.*, 1939, **72**, 1387.

⁵⁷ *Ber.*, 1936, **69**, 1757.

⁵⁸ *Ber.*, 1937, 70, 1894.

⁵⁰ U.S.P. 2,175,843; *Chem. Abstr.*, 1940, **34**, 1036.

⁸⁰ A. Lapworth, *J.*, 1901, **79**, 1276; B. Prager, *Annalen*, 1904, **338**, 375.

⁶¹ W. Borsche and R. Manteuffel, *Ber.*, 1932, **65**, 868; *Annalen*, 1933, **505**, 177.

study of the reaction conditions⁶² has revealed that condensation is best effected in the presence of potassium or rubidium ethoxide with the most careful exclusion of water and oxygen, and that with the higher esters the presence of pyridine is essential. Alcoholysis of the ester groups always takes place during the final facile 1 : α -elimination of acetic acid from (XXXV). Reduction of the enol-acetate of the oxalo-ester (XXXIV) proceeds according to Thiele's rule, but the expected dihydroacetyl compound (XXXV) is frequently accompanied to a greater or lesser extent by the corresponding dihydro-compound in which the acetoxy-group of (XXXV) has been replaced by hydrogen.⁶³ This limitation of the oxalic ester synthesis can sometimes be overcome by aerial oxidation of the dihydro-ester in pyridine solution in the presence of alkali, as was observed with the dihydro-derivatives of methylbixin and crocetin dimethyl ester.⁶⁴ The final stage in the synthesis of *des*-crocetin (crocetin without the four side chain methyl groups) (XXXII; $n = 7$) was thus achieved.¹⁶ Polyene dibasic acids containing side-chain methyl groups have also been synthesised by the oxalic ester method,^{57, 58, 63} and a series of vinyl homologues of glutaconic acid (XXXVI; $n = 2, 3$, and 4) is obtained by oxidation of the oxalo-acids (XXXIII) with hydrogen peroxide.⁶²



The well known ω -oxidation of fatty acids in the animal body takes place more readily with polyene carboxylic acids, and a novel method of converting these acids into the dicarboxylic acids containing the same number of carbon atoms, $\text{CH}_3\cdot[\text{CH}:\text{CH}]_n\cdot\text{CO}_2\text{H} \longrightarrow \text{CO}_2\text{H}\cdot[\text{CH}:\text{CH}]_n\cdot\text{CO}_2\text{H}$ has been developed.^{65, 66} After free or substituted amides of the monocarboxylic acids have been fed to dogs, as much as 20—42% of the monoamide of the dicarboxylic acid ($n = 2, 3$, and 4) can be isolated from the urine. This highly specific biological oxidation phenomenon has also been observed with furancarboxylic acids.

Syntheses based on β -Ionone.

Many attempts to synthesise vitamin A (I) or useful intermediates such as β -ionylideneacetaldehyde (III) have been made, β -ionone being used as starting material, especially by Grignard or similar reactions. Whereas α -ionone reacts normally (1 : 2-addition) with either allyl bromide⁵¹ or with 1-bromo-4-methyl- $\Delta^{2:4}$ -hexadiene ($\text{CH}_2\text{Br}\cdot\text{CH}:\text{CH}\cdot\text{CMe}:\text{CHMe}$)⁶⁷ in the presence of magnesium to give tertiary carbinols, with β -ionone and allyl bromide⁵¹ no carbinol is obtained, the anomalous reaction being attributed to 1 : 4-addition. Abnormal reactions have also been observed

⁶² C. Grundmann, *Ber.*, 1937, **70**, 1148.

⁶³ R. Kuhn and J. Michel, *Ber.*, 1938, **71**, 1119.

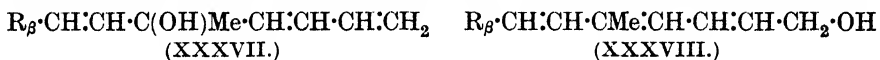
⁶⁴ R. Kuhn and P. J. Drumm, *Ber.*, 1932, **65**, 1458.

⁶⁵ R. Kuhn, F. Köhler, and L. Köhler, *Z. physiol. Chem.*, 1937, **247**, 197.

⁶⁶ See also *idem*, *ibid.*, 1938, **242**, 171.

⁶⁷ N. A. Milas and A. McAlevy, *J. Amer. Chem. Soc.*, 1935, **57**, 580.

with methyl- and phenyl-magnesium halides ⁶⁸ and A. Giacalone ⁶⁹ claims that methane is evolved and ionenes are formed when β -ionone reacts with methylmagnesium iodide. The action of 1:4-dibromo- Δ^2 -butene or 1:2-dibromoethane on β -ionone in the presence of magnesium merely effects reduction to the corresponding pinacol, $C_{26}H_{42}O_2$.⁷⁰ ψ -Ionone appears to react normally with butane-1:4-dimagnesium bromide, leading after dehydration to a dehydrosqualene.⁷¹ The above observations make it necessary to regard with caution Grignard reactions carried out with β -ionone from which it has been claimed (usually on insufficient evidence) that the normal products have been isolated. It has been reported ⁷² that β -ionone reacts with the Grignard compound from bromoacetal $[CH_2Br \cdot CH(OEt)_2]$ giving, after hydrolysis, a 50—60% yield of β -ionylideneacetaldehyde (III), but no evidence is cited to support this claim and there is no indication in the literature that Grignard reactions can be effected with bromoacetal. The condensation of vinyl-⁷³ and divinylacetylenyl-magnesium bromides ⁷⁴ with β -ionone has been described and A. F. Thompson, N. A. Milas, and I. Rovno ⁷⁵ have made a study of the Grignard reaction between β -ionone and various vinylacetylenes; normal reactions apparently ensued and partial reduction yielded alcohols such as (XXXVII), none of which exhibited biological activity, and attempted



isomerisation to the primary alcohols (XXXVIII) failed. Using lithium instead of magnesium, F. B. Kipping and F. Wild ⁶⁸ obtained the normal carbinols (XXXIX; $R = Me$ or Ph) from β -ionone and methyl iodide or bromobenzene, their constitutions being proved by Zerewitinoff determin-

(XXXIX.) $R_\beta \cdot CH:CH \cdot C(OH)MeR \quad CH_2Br \cdot CH:CH \cdot CMe \cdot CH \cdot CH_2 \cdot OMe$ (XL.)

ations and by the isolation of geronic acid on ozonolysis. The same authors,⁷⁶ using lithium, also condensed the bromo-ether (XL) with β -ionone and claimed to have prepared vitamin A methyl ether by dehydration of the resulting tertiary carbinol, but no details of this work or the results of biological tests have yet been published.

β -Ionylideneacetic ester (XLI), prepared by a Reformatsky reaction on β -ionone with ethyl bromoacetate,^{51, 69} the intermediate hydroxy-ester being dehydrated on distillation, has received much attention as an intermediate for vitamin A synthesis. The ester is a mixture of isomers and

⁶⁸ F. B. Kipping and F. Wild, *J.*, 1940, 1239.

⁶⁹ *Gazzetta*, 1937, 67, 464.

⁷⁰ V. Teterin and A. Ivanov, *Compt. rend. Acad. Sci. U.R.S.S.*, 1935, 2, 259.

⁷¹ J. Schmidt, *Annalen*, 1941, 547, 115.

⁷² M. V. Krauze and J. M. Slobodin, *J. Gen. Chem. Russia*, 1940, 10, 907.

⁷³ J. Salkind, S. Zonis, and N. Blochin, *Compt. rend. Acad. Sci. U.R.S.S.*, 1935, 2, 57.

⁷⁴ J. Salkind and S. Zonis, *Russ. P.*, 51,905; *Chem. Zentr.*, 1938, II, 768.

⁷⁵ *J. Amer. Chem. Soc.*, 1941, 63, 752.

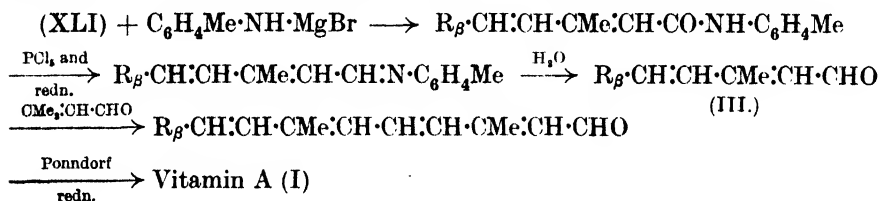
⁷⁶ *Chem. and Ind.*, 1939, 802; *Ann. Reports*, 1939, 36, 337.

yields on hydrolysis only a small quantity of a crystalline acid; this same isomer is also obtained by hydrolysis of the nitrile resulting from a cyano-acetic ester condensation with β -ionone.⁵⁶ The saturated ester from the catalytic hydrogenation of (XLI) was used for the well-known synthesis of perhydrovitamin A.⁷⁷ By reaction of β -ionylideneacetyl chloride with



methylzinc iodide, P. Karrer and R. Morf⁷⁸ prepared the triethenoid ketone, β -euionone (XLII), and the corresponding alcohol, both of which, although they give blue colours with antimony trichloride in chloroform, are biologically inactive. Dry distillation of the barium salt of β -ionylideneacetic acid⁷⁹ with barium formate yielded a C_{15} aldehyde and attempts were made⁸⁰ to employ this method to extend the chain towards vitamin A. The absorption spectra⁷⁹ of the aldehyde, however, and of its derivatives⁸¹ indicate that it has a structure different from that of the expected β -ionylideneacetaldehyde (III).

Material possessing growth-promoting properties has been obtained by R. Kuhn and C. J. O. R. Morris⁸² by carrying out the synthesis outlined below, starting with β -ionylideneacetic ester (XLI). Reduction of the imido-chloride by the chromous chloride method of von Braun³⁵ furnished a C_{15} -aldehyde which is assumed to have the structure (III). The absorption spectrum¹ of its crystalline semicarbazone would appear to indicate that



the aldehyde is β -ionylideneacetaldehyde (III), but similar absorption spectra are exhibited by the bicyclic C_{15} aldehydes obtained by I. M. Heilbron and his collaborators,³⁸ and it must be borne in mind that even in the simple case of citrylideneacetic acid, the chromous chloride method fails to yield the normal citrylideneacetaldehyde (p. 175). Completion of the synthesis as outlined above and purification of the product by chromatographic analysis gave a final product which, estimated by the antimony trichloride method, contained 7.5% of vitamin A, and which, when tested biologically on this basis, gave similar growth responses to the natural vitamin. P. Karrer and A. Rüegger⁸³ experienced difficulty in repeating the Kuhn synthesis but unfortunately did not prepare a semicarbazone

⁷⁷ P. Karrer and K. Schöpp, *Helv. Chim. Acta*, 1933, **16**, 625.

⁷⁸ *Ibid.*, 1934, **17**, 3.

⁷⁹ W. H. Davies, I. M. Heilbron, W. E. Jones, and A. Lowe, *J.*, 1935, 584.

⁸⁰ I. M. Heilbron, W. E. Jones, A. Lowe, and H. R. Wright, *J.*, 1936, 561.

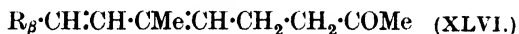
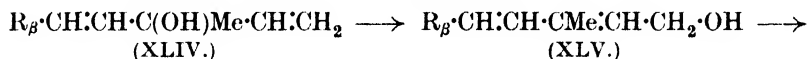
⁸¹ A. Burawoy, *J.*, 1941, 20.

⁸² *Ber.*, 1937, **70**, 853; U.S.P. 2,239,491; *Chem. Abstr.*, 1941, **35**, 4918.

⁸³ *Helv. Chim. Acta*, 1940, **23**, 284.

of the C_{15} aldehyde which they obtained. According to these authors the main product of the Kuhn synthesis differs from vitamin A chromatographically and in the location of the absorption maximum of the antimony trichloride coloration. Other workers⁷² have reported that the Kuhn synthesis gives biologically inactive products.

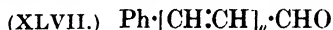
Alternative routes to the C_{15} aldehyde (III) and the corresponding alcohol (XLV) appeared to be feasible from the acetylene carbinol (XLIII) of



β -ionone. This has been prepared by condensation of β -ionone with acetylene in the presence of sodamide⁷⁹ or potassium *tert.*-amyloxide,⁸⁴ the latter method affording a mixture of the normal carbinol (XLIII) and the 1:4-addition product. No aldehyde could be obtained from (XLIII) by treatment with either formic acid or acetic anhydride,^{79, 80} but the alcohol (XLV) was obtained from the vinyl carbinol (XLIV) with either acetic anhydride or trichloroacetic acid.⁸⁴ Condensation of the corresponding bromide with ethyl sodioacetoacetate yielded a C_{18} ketone (XLVI), from which, by repetition of the acetylene synthesis, a biologically inactive dihydrovitamin A was prepared.

Phenyl Polyene Aldehydes.

The earliest study of the preparation of these aldehydes (XLVII) is due to G. Engleberg,⁸⁵ who condensed cinnamaldehyde with acetaldehyde



in the presence of dilute alkali solution and obtained phenylpentadienal (XLVII; $n = 2$) and the trienal (XLVII; $n = 3$) as crystalline solids, although in rather poor yield. Phenylpentadienal in 10% yield is also obtained from benzaldehyde and crotonaldehyde, 30% alkali solution⁸⁶ or piperidine acetate⁸ being used as catalyst, or from cinnamaldehyde and acetaldehyde by means of sodamide.³⁴ Application of the stannous chloride reduction method⁸⁷ to phenylpolyene nitriles^{56, 88} gave a 40% yield of cinnamaldehyde and a 10% yield of phenylpentadienal (XLVII; $n = 2$) from the corresponding nitriles, but an attempt to prepare the trienal (XLVII; $n = 3$) failed completely. R. Kuhn and K. Wallenfels⁴⁶ condensed cinnamaldehyde and crotonaldehyde in the presence of piperidine acetate and by taking advantage of their different solubilities in benzene

⁸⁴ R. G. Gould and A. F. Thompson, *J. Amer. Chem. Soc.*, 1935, **57**, 340; R. G. Gould, *J. Biol. Chem.*, 1936, **114**, xli.

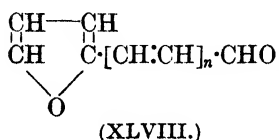
⁸⁵ Dissert., Berlin University, 1914; see also D. Vorländer, E. Fischer, and K. Kunze, *Ber.*, 1925, **58**, 1284; D. Vorländer and E. Daehn, *Ber.*, 1929, **62**, 541.

⁸⁶ R. Kuhn and A. Winterstein, *Helv. Chim. Acta*, 1929, **12**, 493.

⁸⁷ H. Stephen, *J.*, 1925, **127**, 1874.

⁸⁸ G. Wittig and R. Kethur, *Ber.*, 1936, **69**, 2078.

were able to isolate phenylundecapentaenal (XLVII; $n = 5$) in 3% yield, along with a trace of the very sparingly soluble phenylpentadecaheptaenal (XLVII; $n = 7$). These yields have been improved considerably by J. Schmidt,⁸⁹ who, using higher proportions of crotonaldehyde and catalyst, working in 70% alcohol, and allowing the reaction to proceed for several days, achieved a 50% yield of the trienal (XLVII; $n = 3$), together with a 20% yield of the pentaenal (XLVII; $n = 5$). Similarly, phenylpentadienal and crotonaldehyde gave good yields of phenyltridecahexaenal (XLVII, $n = 6$) (insoluble in benzene) and phenylnonatetraenal (XLVII; $n = 4$), and phenylpentadecaheptaenal (XLVII; $n = 7$) was obtained in excellent yield from the pentaenal with crotonaldehyde. Schmidt suggests that the more unsaturated the aldehyde the more rapidly and smoothly the aldehyde

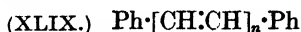


group condenses with the terminal methyl group of crotonaldehyde. By alkali-catalysed condensation of furfural with acetaldehyde, W. König⁹⁰ prepared a series of furyl polyene aldehydes (XLVIII; $n = 1, 2$, and 3) and Schmidt,⁸⁹ using the elegant piperidine acetate method, has not only

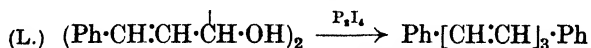
obtained much better yields of the simpler aldehydes, but has also synthesised a number of the higher members (XLVIII; $n = 4, 5, 6$, and 7).

Diphenyl Polyenes.

Our knowledge of this series, the most widely studied in the polyene field, is due mainly to the Heidelberg school, which has achieved the synthesis of a member containing as many as fifteen conjugated double bonds (XLIX; $n = 15$). Only a brief survey of the four main methods used can be given here.



(1) 1 : 2-Glycols such as hydrocinnamoin (L), when treated with phosphorus di-iodide in ether, give the diphenyl polyene in almost quantitative yield⁹¹ and this method has now been extended⁹² to the 1 : 4- and 1 : 6-glycols obtainable from condensations with acetylene and diacetylene.



With acetylene glycols from ketones, diphenyl polyenes with side-chain methyl groups are obtainable, although reduction has here to be effected with chromous chloride or vanadium dichloride rather than with phosphorus di-iodide.

(2) By condensation of cinnamaldehyde with sodium succinate in acetic anhydride, R. Fittig and L. Batt⁹³ obtained minute and inconsistent yields of 1 : 8-diphenyloctatetraene (XLIX; $n = 4$). This method was vastly improved and made generally applicable to diphenyl polyene synthesis by

⁸⁹ *Annalen*, 1941, **547**, 270.

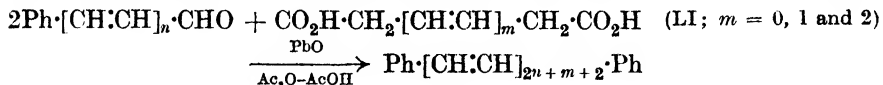
⁹⁰ *Ber.*, 1925, **58**, 2559.

⁹¹ R. Kuhn and A. Winterstein, *Helv. Chim. Acta*, 1928, **11**, 87.

⁹² R. Kuhn and K. Wallenfels, *Ber.*, 1938, **71**, 1889.

⁹³ *Annalen*, 1904, **331**, 152.

the discovery by R. Kuhn and A. Winterstein⁹¹ that with lead oxide in boiling acetic acid-acetic anhydride a homogeneous solution can be obtained in which the aldehyde and the acid rapidly condense, giving the diphenyl polyene in good yield. The general method, indicated below, only breaks down when applied to the synthesis of polyenes higher than 1:16-diphenyl-



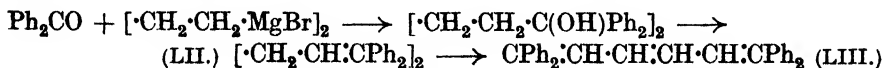
hexadecaoctaene (XLIX; $n = 8$). The synthesis can be extended to butadiene-1:4-diacetic acid (LI; $m = 2$), prepared by the oxalic ester method, which condenses with cinnamaldehyde, yielding 1:12-diphenyldodecahexaene (XLIX; $n = 6$).⁵⁷ Diphenyl polyenes with side-chain methyl groups have also been prepared in this way⁹⁴ from methylcinnamaldehyde.

(3) Dehydration of the secondary carbinols formed by condensation of benzylmagnesium chloride with phenyl polyene aldehydes provides yet another method of phenyl polyene synthesis.⁴⁶

(4) An entirely novel route which has permitted considerable extension of this series involves the elimination of sulphur or selenium from polyene thio- and seleno-aldehydes⁹⁵ under the influence of various reagents. No experimental details have as yet been published, but 1:22-diphenyldocosaundecaene (XLIX; $n = 11$) and 1:30-diphenyltricontapentadecaene (XLIX; $n = 15$) have been synthesised in this way from 11-phenylundecapentaenal and 15-phenylpentadecaheptaenal respectively. An unusual type of diphenyl polyene, 4:5-diphenyloctatetraene, was obtained⁹⁶ by fusion of the pinacol from 3-benzoylpropyl bromide with sulphanilic acid.

The stability of the diphenyl polyenes and of the higher phenyl polyene aldehydes is remarkable and it is largely solubility difficulties which hinder the further extension of these series. R. Kuhn and A. Winterstein⁹¹⁻⁹⁷ have made a detailed study of the reactions of the diphenyl polyenes, particularly in connection with the addition of hydrogen and bromine.

G. Wittig and A. Klein⁹⁸ have prepared, mainly by method (2) above, a series of $\omega\omega'$ -tetraphenyl polyenes, and have examined the behaviour of these compounds, even more stable than the diphenyl polyenes, towards oxygen and bromine. The diacetyleneglycol-phosphorus di-iodide method has also been utilised for the synthesis of a member of this series, 1:1:6:6-tetraphenylhexatriene (LIII).⁹² J. Schmidt⁹⁹ obtained the same hydro-



carbon (LIII) by dehydrogenation of the diene (LII) with selenium dioxide, and similarly, he prepared 1:6-diphenylenehexatriene from fluorenone,

⁹⁴ K. Bernhauer and I. Skudrzyk, *J. pr. Chem.*, 1940, **155**, 310.

⁹⁵ R. Kuhn, *J.*, 1938, 605; *Angew. Chem.*, 1937, **50**, 703.

⁹⁶ S. N. Chitrik, *J. Gen. Chem. Russia*, 1940, **10**, 2095.

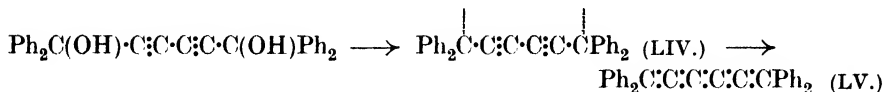
⁹⁷ *Helv. Chim. Acta*, 1928, **11**, 123, 144.

⁹⁸ *Ber.*, 1936, **69**, 2087.

⁹⁹ *Annalen*, 1941, **547**, 103.

previously synthesised along with another member of the series by the lead oxide method¹ and later by the diacetylene-phosphorus di-iodide synthesis.⁹²

Closely related to the polyenes are the cumulenes, compounds containing an unbroken sequence of double bonds, :C:C:C:C: . R. Kuhn and K. Wallenfels² have developed a neat synthesis which involves treatment of acetylenic or diacetylenic glycols with chromous chloride in the presence of hydrogen chloride. In this way the diacetyleneglycol from



benzophenone yields the scarlet tetraphenylhexapentaene (LV) in 93% yield, presumably by way of an electronic rearrangement of the double radical (LIV). The cumulenes absorb at longer wave-lengths than the corresponding polyenes with the same number of double bonds, and interesting differences in chemical properties have been observed.

Absorption Spectra.

It is only possible to give here a brief indication of the application of light absorption measurements in the synthetic polyene series. A valuable general account of absorption spectrophotometry has been given by R. A. Morton³ and a collection of very useful data, including many of the results obtained with polyenes, has been made by K. Dimroth⁴ in an article on the relation between ultra-violet absorption spectra and the constitution of organic compounds. The first comprehensive study of the absorption spectra of synthetic polyenes was made by K. W. Hausser, R. Kuhn, and their co-workers,⁵ although some observations on the correlation of light absorption and constitution of the furyl polyene aldehydes were made by W. König⁹⁰ in 1925. It has been found⁵ that absorption maxima are progressively displaced towards longer wave-lengths with increasing conjugation of ethenoid linkages and that the displacement diminishes with each additional conjugation. This is clearly illustrated by the figures for the diphenyl polyenes.¹

No. of double bonds (n) ...	5	6	7	11	15
Max. in PhNO_2	4340	4580	4740	5300	5700 Å.

The intensity of absorption (molecular extinction coefficient, ϵ), on the other hand, exhibits a strictly linear variation with the number of conjugated linkages. R. Kuhn and C. Grundmann¹⁶ have elaborated some valuable rules for symmetrical polyenes. These include the equivalence of

¹ R. Kuhn and A. Winterstein, *Helv. Chim. Acta*, 1928, **11**, 116.

² *Ber.*, 1938, **71**, 783, 1510; see also R. Kuhn and G. Platzer, *Ber.*, 1940, **73**, 1410.

³ "Practical Aspects of Absorption Spectrophotometry," Institute of Chemistry, London, 1938.

⁴ *Angew. Chem.*, 1939, **52**, 545.

⁵ *Z. physikal. Chem.*, 1935, **B**, **29**, 363, 371, 378, 391, 417.

conjugated carbonyl and phenyl groups to one and one and a half ethenoid linkages respectively, and side-chain methyl groups cause a displacement towards the visible equivalent to one quarter of that produced by an ethenoid linkage. A. Burawoy⁸¹ has summarised the spectrographic results which were largely employed in elucidating the constitution of several C_{14} and C_{15} aldehydes by I. M. Heilbron and his co-workers.^{33, 34, 37}

Although our knowledge of the relationship between light absorption and constitution is still essentially empirical in character, sufficient information is now available to make absorption spectra determinations practically indispensable in the polyene series and invaluable in many other branches of organic chemistry.

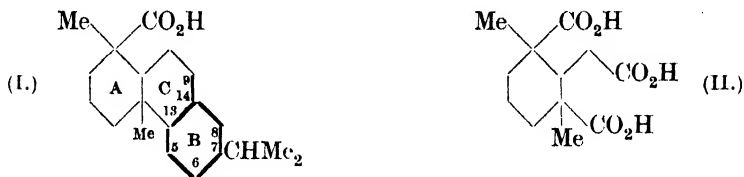
E. R. H. J.

6. POLYTERPENES.

This review is limited to a discussion of the chemistry of abietic acid and of the β -amyrin and lupeol triterpene sub-groups. A consideration of the α -amyrin triterpene sub-group is deferred, first, because of space limitations and, secondly, because structural investigations within this field, although numerous, have not reached a sufficiently advanced stage.

Diterpenes.

Abietic Acid.—The structure of abietic acid has been established by chemical as distinct from physical methods. In 1938, the acid was represented by the general formula (I), the two ethylenic linkages occupying positions within the thick type. The general location of the two ethylenic



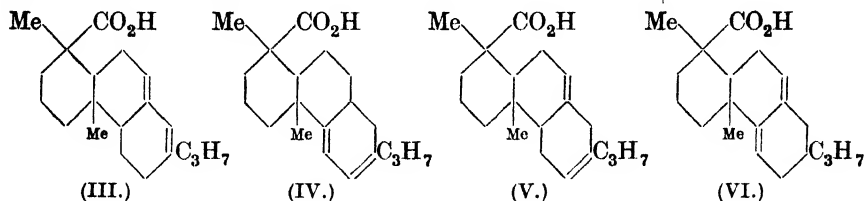
linkages is established by the observation that oxidation of abietic acid with potassium permanganate gives the tricarboxylic acid $C_{12}H_{18}O_6$ (II).¹ The formation of an abietic acid-maleic anhydride adduct² was assumed to indicate that the ethylenic linkages are present as a conjugated system in ring B. Furthermore, since isobutyric acid is among the products of oxidation of abietic acid with either permanganate or ozone, the conjugated system probably includes C_7 . Later, however,³ it was shown that the formation of a maleic anhydride adduct was not a simple reaction, and that the adduct originates in *laevopimaric* acid. Various locations [within the general structure (I)] for the unsaturated centres have been advocated;

¹ L. Ruzicka, M. W. Goldberg, H. W. Huyser, and C. F. Seidel, *Helv. Chim. Acta*, 1931, **14**, 545.

² L. Ruzicka, P. J. Ankersmit, and B. Frank, *ibid.*, 1932, **15**, 1289.

³ L. Ruzicka and R. G. R. Bacon, *J. Soc. Chem. Ind.*, 1936, **55**, 546.

of these, (III) was suggested by F. Vocke⁴ and preferred by L. F. Fieser⁵ and W. Sandermann.⁶ This structure receives confirmation from the observation that the acid (II) is not accompanied by a higher homologue which would be expected if both ethylenic linkages were in ring B. On the other hand, K. Schultz⁷ preferred (IV), since oxidation of abietic acid gives 0.9 mol. of oxalic acid.



K. Kraft⁸ showed that abietic acid exhibits an intense absorption maximum at 2370 μ , from which he concluded that the ethylenic linkages are conjugated. L. F. Fieser⁵ concluded that the location of the absorption maximum indicates that abietic acid contains a conjugated system spread over two condensed rings as in (III). As chemical evidence of conjugation in abietic acid, L. F. Fieser and W. P. Campbell⁹ found that the acid couples with diazotised *p*-nitroaniline. L. Ruzicka and L. Sternbach,¹⁰ however, point out that such a coupling would be possible if abietic acid possessed structure (V), although such a formula appears unlikely on spectroscopic grounds. The alternative formula (VI) gives a reasonable explanation of the behaviour of abietic acid with the exception of the formation of isobutyric acid.

At this stage, a re-examination of the degradation of abietic acid was undertaken with the object of differentiating between the more or less probable structures (III)–(VI). By controlled oxidation of abietic acid with permanganate, P. Levy¹¹ obtained α -tetrahydroxyabietic acid, m. p. 248–250°, and later,¹² an “isomeric tetrahydroxyabietic acid,” m. p. 208–210°. L. Ruzicka and J. Meyer,¹³ using the same method, obtained a dihydroxyabietic acid, and later L. Ruzicka and L. Sternbach¹⁰ showed that both the dihydroxy- and the α -tetrahydroxy-acid can be isolated from the reaction mixture. The α -tetrahydroxy-acid is probably formed *via* an oxidodihydroxyabietic acid, since the initial oxidation product is converted by hydrochloric acid into a chlorotrihydroxyabietic acid from which an oxidodihydroxy-acid is again obtained on treatment with alkali. Oxidation of α -tetrahydroxyabietic acid with lead tetra-acetate gave an amorphous product, which on further oxidation with sodium hypobromite gave an optically active tetracarboxylic acid, $C_{15}H_{22}O_8$.¹⁰ In the light of the

⁴ *Annalen*, 1932, **497**, 247.

⁵ “Natural Products related to Phenanthrene,” New York, 2nd Edn., pp. 344–347.

⁶ *Bull. Inst. Pin.*, 1937, (3), 138.

⁷ *Coll. Czech. Chem. Comm.*, 1937, **9**, 542.

⁸ *Annalen*, 1935, **520**, 138.

⁹ *J. Amer. Chem. Soc.*, 1938, **60**, 159.

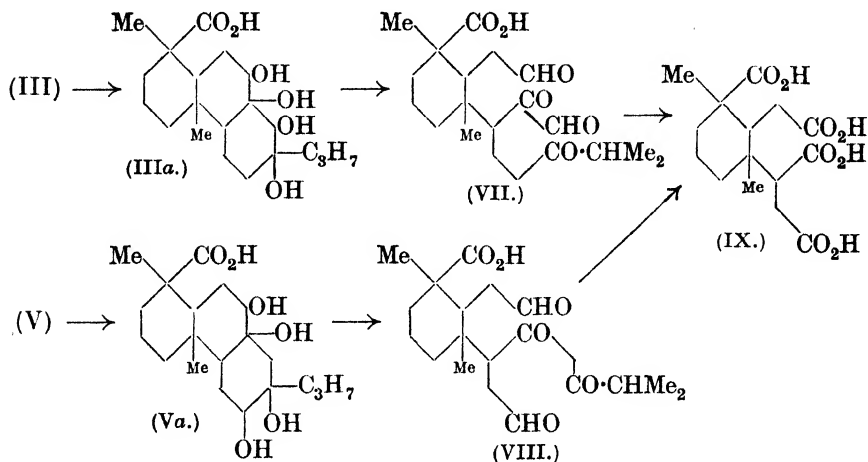
¹⁰ *Helv. Chim. Acta*, 1938, **21**, 565.

¹¹ *Ber.*, 1909, **42**, 4305.

¹² *Ibid.*, 1926, **59**, 1302.

¹³ *Helv. Chim. Acta*, 1923, **6**, 1097.

established structure of the tricarboxylic acid (II), this tetracarboxylic acid must have the structure (IX), which thus limits the formula of abietic



acid to either (III) or (V). Accordingly, the α -tetrahydroxy-acid will be either (IIIa) or (Va) and the amorphous oxidation product (VII) or (VIII). The tetracarboxylic acid (IX) gives a dimethyl ester (esterification of the two primary carboxyl groups) when treated with methyl-alcoholic hydrogen chloride in the cold, a trimethyl ester (esterification of the two primary and the secondary carboxyl groups) when boiled with the same reagent, and a tetramethyl ester with diazomethane. This series of changes clearly proves that one of the ethylenic linkages of abietic acid is situated between C₉ and C₁₄.

The exact location of the second ethylenic linkage of abietic acid has been deduced from a study of dihydroxyabietic acid.¹⁴ This acid has been related to α -tetrahydroxyabietic acid (IIIa) or (Va), since on oxidation with permonophthalic acid it gives an oxide,* hydration of which gives the α -tetrahydroxy-acid. One of the hydroxyl groups of dihydroxyabietic acid is attached to C₇, since dehydrogenation with selenium or palladised charcoal gives 7-hydroxy-1-methylphenanthrene (X) in addition to retene.¹⁵ Moreover, the two hydroxyl groups of dihydroxyabietic acid must form an α -glycol grouping, since on oxidation with lead tetra-acetate the dihydroxy-acid (XI) gives an unsaturated keto-aldehyde (XII), which with alkali yields a keto-diene acid the properties of which, including the absorption spectrum, agree with the formula (XIII); this degradation does not exclude the alternative 6 : 7-dihydroxy-structure for dihydroxyabietic acid.

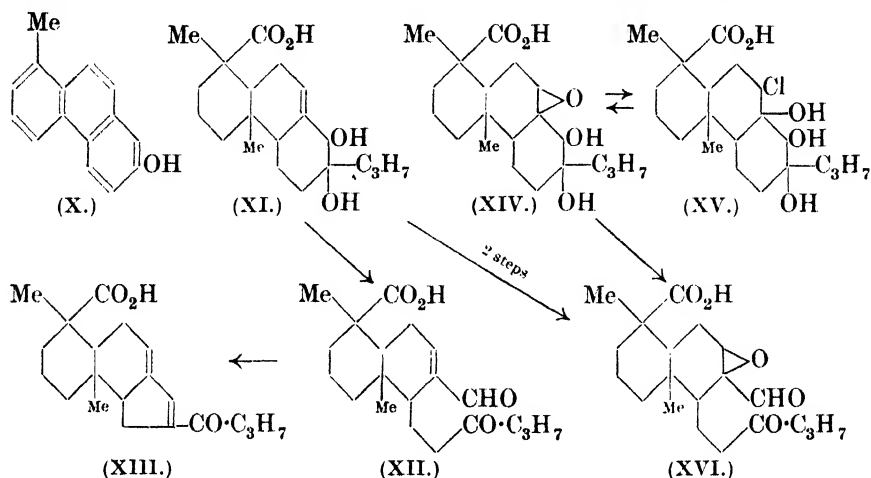
The relationship of the oxido-dihydroxy-acid (XIV), obtained from chlorotrihydroxyabietic acid (XV), and the dihydroxy-acid has been estab-

¹⁴ L. Ruzicka and L. Sternbach, *Helv. Chim. Acta*, 1940, **23**, 333, 341.

¹⁵ *Idem, ibid.*, p. 355.

* This oxide was not obtained pure; it is possible that it is stereoisomeric with the oxide obtained from chlorotrihydroxyabietic acid.

lished by oxidation with lead tetra-acetate; an oxido-keto-aldehyde (XVI) was thus obtained identical with the product obtained by oxidation of (XI) first with permanganic acid and then with lead tetra-acetate.¹⁴



Treatment of the oxido-dihydroxy-acid (XIV) with boiling toluene converts it into an inner dimeric ester of α -tetrahydroxyabiatic acid (XVII) in which the carboxyl group of one abiatic residue is esterified by the hydroxyl group of another.¹⁶ When oxidised with lead tetra-acetate (2 mols. per abiatic residue), (XVII) is converted into a diketone-inner ester (XVIII) with loss of one carbon atom from each abiatic residue. This degradation shows that the inner dimeric ester (XVII) contains a glycerol grouping in each abiatic residue, and therefore proves that in α -tetrahydroxyabiatic acid the four hydroxyl groups are attached to adjacent carbon atoms. Thus structure (V) is eliminated and formula (III) correctly represents abiatic acid.

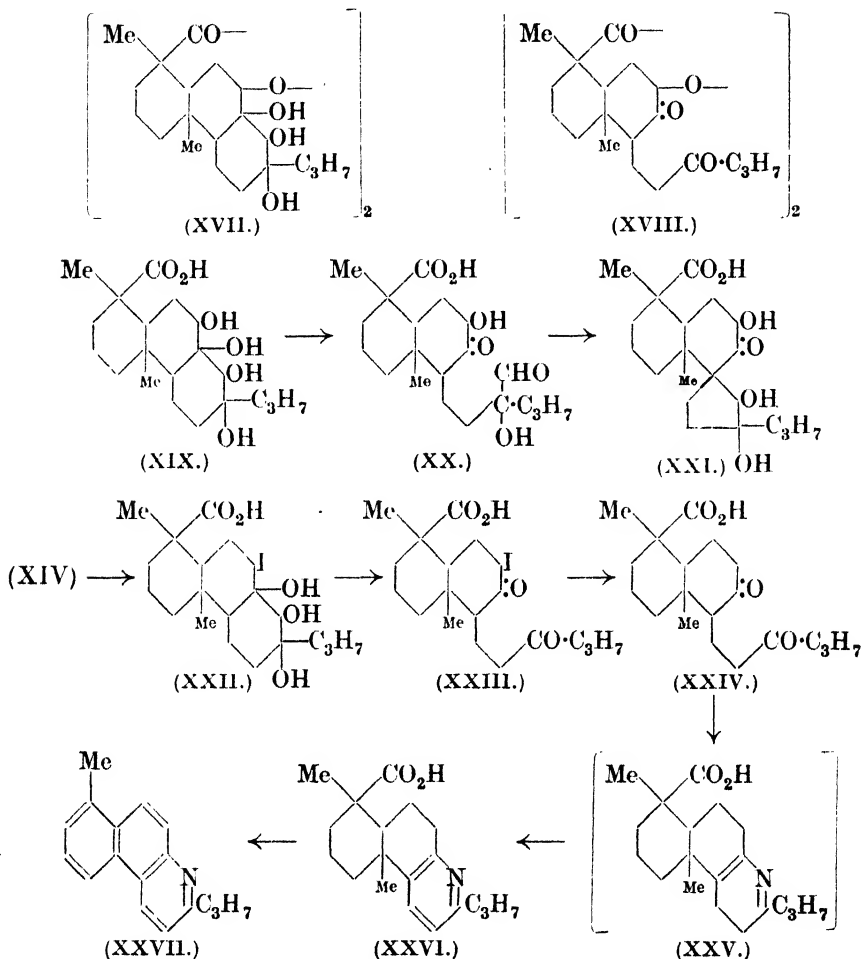
The "isomeric tetrahydroxyabiatic acid," m. p. 208—210°, of P. Levy is an oxidation product of α -tetrahydroxyabiatic acid and is to be formulated as (XXI),¹⁶ since it is obtained from the primary product (XX) of oxidation of α -tetrahydroxyabiatic acid (XIX) with 1 mol. of lead tetra-acetate, by treatment with acid or alkali.

Finally, the problem of the elucidation of the exact positions of the ethenoid linkages of abiatic acid has been brought within reach of synthetic solution by a remarkable series of reactions described by L. Ruzicka, L. Sternbach, and O. Jeger.¹⁷ Treatment of the oxidodihydroxy-acid (XIV) with hydriodic acid gives the iodo-trihydroxy-acid (XXII), which with lead tetra-acetate gives the iodo-diketo-acid (XXIII) with loss of one carbon atom (a reaction which incidentally proves that the iodo-trihydroxy-acid is a glycerol). Replacement of the halogen atom by hydrogen (hydriodic

¹⁶ L. Ruzicka and L. Sternbach, *Helv. Chim. Acta*, 1941, **24**, 223.

¹⁷ *Ibid.*, p. 504.

acid) yields the diketo-acid (XXIV), which on treatment with ammonia gives a pyridine derivative—azadehydroabietic acid (XXVI)—which is



probably formed by disproportionation (or oxidation) of the intermediate dihydropyridine derivative (XXV). Azadehydroabietic acid is soluble in acids and alkalis, it yields a picrate and its absorption spectrum is similar to that of a substituted pyridine. Dehydrogenation of (XXVI) with selenium yields 8-azaretene (XXVII); a proof of the structure of 8-azaretene by synthesis will afford unequivocal evidence of the correctness of formula (III) for abietic acid.

Triterpenes.

The period reviewed¹⁸ has been largely devoted to establishing relationships between individual triterpenes; polycyclic triterpenes can now be

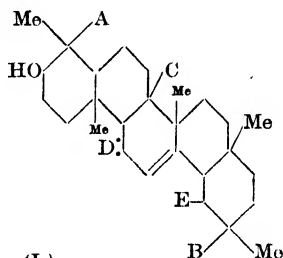
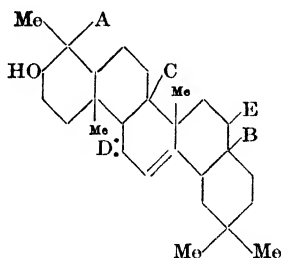
¹⁸ *Ann. Reports*, 1937, **34**, 327.

classified into three groups, the members of each group being directly related to each other :

I. *β*-Amyrin Group.

	A.	B.	C.	D.	E.
(Ia) <i>β</i> -Amyrin	CH ₃	CH ₃	CH ₃	H ₃	H
(Ib) Erythrodol	CH ₃	CH ₃ ·OH	CH ₃	H ₃	H
(Ic) Oleanolic acid	CH ₃	CO ₂ H	CH ₃	H ₃	H
(Id) <i>α</i> -Boswellic acid.....	CO ₂ H	CH ₃	CH ₃	H ₃	H
(Ie) Hederagenin	CH ₃ ·OH	CO ₂ H	CH ₃	H ₃	H
(If) Gypsogenin	CHO	CO ₂ H	CH ₃	H ₃	H
(Ig) Glycyrrhetic acid	CH ₃	CH ₃	CO ₂ H	:O	H
(Ih) Echinocystic acid	CH ₃	CO ₂ H	CH ₃	H ₃	OH
(Ii) Quillaic acid	CHO	CO ₂ H	CH ₃	H ₃	OH

Basseol



II. *α*-Amyrin Group.

α-Amyrin
Ursolic acid
β-Boswellic acid

III. Lupeol Group.

Lupeol
Betulin

The inter-relationships have for the most part been determined by the application of a method developed by L. Ruzicka and co-workers in which monocarboxylic acid members of the group are converted into the corresponding aldehyde by the Rosenmund method (the hydroxyl group being protected), and the aldehyde then reduced to the corresponding deoxo-compound by the Kishner-Wolff method. Incidentally, the Kishner-Wolff technique has been considerably simplified by G. A. R. Kon and H. R. Soper.¹⁹ Rosenmund reduction of the acetate-acid chloride of oleanolic acid (Ic) gives acetyl oleanol-aldehyde, reduction of which by the Kishner-Wolff method yields a mixture of *β*-amyrin (Ia) and erythrodol (Ib).²⁰ Conversely, the relationship of erythrodol and oleanolic acid is confirmed by the oxidation of the 2-monostearate of the diol to the stearate of oleanolic acid.²¹ *α*-Boswellic acid (Id) has been converted through the corresponding aldehyde into a mixture of *β*-amyrin (Ia)²² and *epi-β*-amyrin.²³ Catalytic reduction of glycyrrhetic acid (Ig), an *αβ*-unsaturated ketone,²⁴

¹⁹ J., 1940, 1335.

²⁰ L. Ruzicka and H. Schellenberg, *Helv. Chim. Acta*, 1937, 20, 1553.

²¹ J. Zimmermann, *ibid.*, 1936, 19, 247.

²² L. Ruzicka and W. Wirz, *ibid.*, 1940, 23, 132.

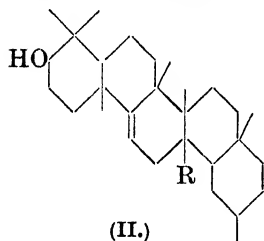
²³ *Idem*, *ibid.*, 1941, 24, 248.

²⁴ L. Ruzicka and S. L. Cohen, *ibid.*, 1937, 20, 804; L. Ruzicka, H. Leuenberger, and H. Schellenberg, *ibid.*, p. 1271.

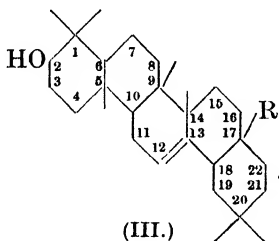
gives the corresponding deoxo-acid; the latter acid is converted into the corresponding aldehyde and thence by Kishner-Wolff reduction into β -amyrin (Ia).²⁵ Gypsogenin (If) has been directly reduced to oleanolic acid (Ic)²⁶ by the Kishner-Wolff method, and, on the other hand, gypsogenin (If) has been catalytically reduced to hederagenin (Ie).²⁷ Echinocystic acid (Ih) has been converted into a hydrocarbon, oleanene III,²⁸ previously obtained from oleanolic acid,²⁹ and quillaic acid has been directly reduced to echinocystic acid.³⁰ The tetracyclic diethenoid basseol has been converted into the pentacyclic monoethenoid β -amyrin by a number of cyclisation reactions.³¹

The members of the smaller α -amyrin group have been inter-related by application of the Ruzicka method; thus, both ursolic acid³² and β -boswellic acid³³ have been converted into α -amyrin. The two members of the third group were inter-related by the direct conversion of the dihydric alcohol betulin into the monohydric alcohol lupeol.³⁴

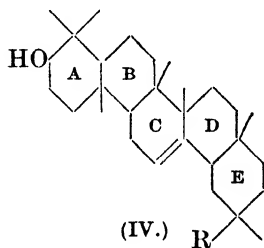
I. β -Amyrin Group.— β -Amyrin and oleanolic acid. A consideration of the dehydrogenation and degradation reactions of members of the β -amyrin group¹⁷ led to the development of the Ruzicka hydropicene structure (II, R = Me) for β -amyrin and (II, R = CO₂H) for oleanolic acid. These representations were quickly found to be unsatisfactory, as they are not compatible with many reactions of the members of the β -amyrin group; these reactions are considered in the sequel. A modification (III) of struc-



(II.)



(III.)



(IV.)

ture (II) suggested by R. D. Haworth³⁵ gives a much more satisfactory representation of the reactions of β -amyrin and oleanolic acid. A further modification (IV) has recently been suggested by P. Bilham and G. A. R. Kon;³⁰ measurements on unimolecular films of the isomeric oleanic acids and the related hedraganic acid (and of their methyl esters) give

²⁵ L. Ruzicka and A. Marxer, *Helv. Chim. Acta*, 1939, **22**, 195.

²⁶ L. Ruzicka and G. Giacomello, *ibid.*, 1936, **19**, 1136.

²⁷ *Idem*, *ibid.*, 1937, **20**, 299.

²⁸ D. Todd, G. H. Harris, and C. R. Noller, *J. Amer. Chem. Soc.*, 1940, **62**, 1624.

²⁹ A. Winterstein and G. Stein, *Annalen*, 1933, **502**, 223.

³⁰ P. Bilham and G. A. R. Kon, *J.*, 1941, 552.

³¹ J. H. Beynon, I. M. Heilbron, and F. S. Spring, *J.*, 1937, 989.

³² J. A. Goodson, *J.*, 1938, 999.

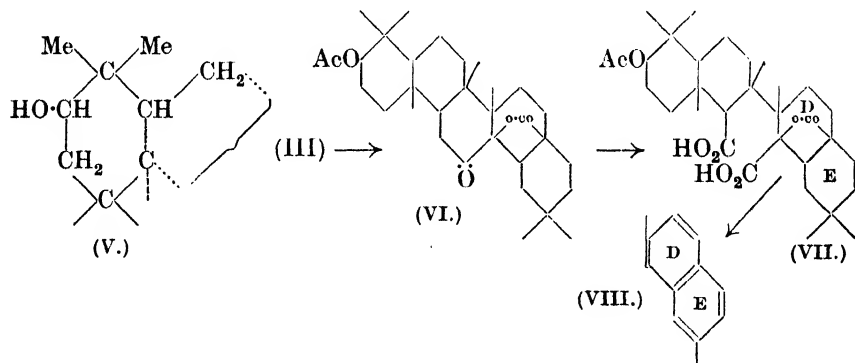
³³ L. Ruzicka and W. Wirz, *Helv. Chim. Acta*, 1939, **22**, 948.

³⁴ L. Ruzicka and M. Brenner, *ibid.*, p. 1523.

³⁵ *Ann. Reports*, 1937, **34**, 338.

values which are incompatible with the presence of a carboxyl group attachment at C₁₇ in oleanolic acid (III, R = CO₂H) and indicate that the carboxyl group is attached to an extremity of the molecule, so leading to the representation (IV, R = CO₂H) for oleanolic acid.

An analysis of the alternative formulæ (III) and (IV) shows that they account for the formation of the products of dehydrogenation of members of the group and in particular for the formation of 1:8-dimethylpicene and of 2-hydroxy-1:8-dimethylpicene. The angular methyl group attached to C₉ is required to account for the formation of 6-hydroxy-1:2:5-trimethylnaphthalene and 1:2:5:6-tetramethylnaphthalene from rings A and B. The angular methyl group at C₁₄ is likewise required to explain the formation of 1:2:7-trimethylnaphthalene and 2:7-dimethylnaphthalene from rings D and E. The formulæ (III) and (IV) furthermore include the system (V), the presence of which in β -amyrin has been established by oxidative degradation of various members of the group.³⁶ The next important step in the elaboration of the hydropicene triterpene structure was a proof that the unsaturated centre of the β -amyrin group is located in ring C. This decision was first dependent upon an observation of L. Ruzicka and K. Hofmann,³⁷ who found that dehydrogenation of acetyloleanolic lactone dicarboxylic acid [(VII), based on (III, R = CO₂H) for oleanolic acid], obtained by oxidation of ketoacetyloleanolic lactone (VI), gave 2:7-dimethylnaphthalene (VIII). In order to confirm that the 2:7-dimethyl-



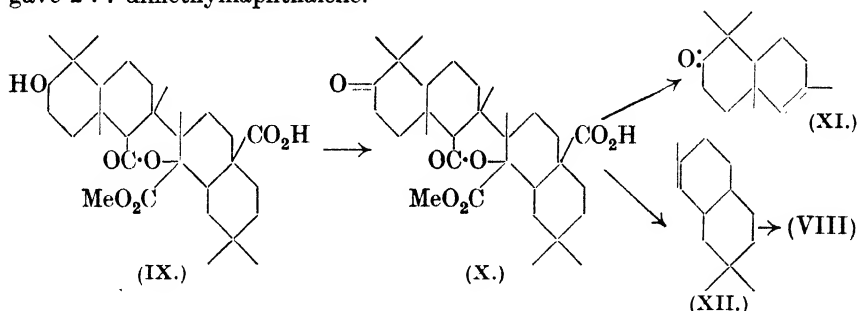
naphthalene fragment originates in rings D and E, an examination was made of the monomethyl ester of isooleanolic lactone dicarboxylic acid (IX), obtained by alkaline hydrolysis of the dimethyl ester of (VII).

Oxidation of (IX) gave the corresponding C₂-ketone (X), pyrolysis of which yielded a hydrocarbon fraction and a ketonic fraction in almost equal amounts. From the former was isolated a ketone (as semicarbazone), C₁₄H₂₂O₇, formulated as (XI). The hydrocarbon fraction is considered to

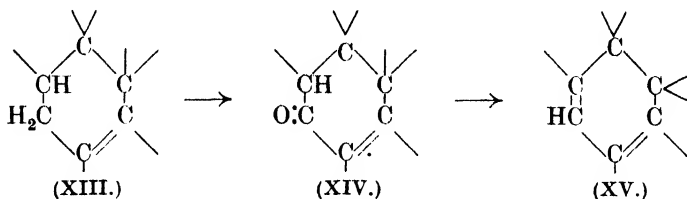
³⁶ W. A. Jacobs and E. L. Gustus, *J. Biol. Chem.*, 1926, **69**, 641; L. Ruzicka and G. Giacomello, *Helv. Chim. Acta*, 1937, **20**, 299.

³⁷ *Helv. Chim. Acta*, 1936, **19**, 124.

contain a substance formulated as (XII). Dehydrogenation of the fraction gave 2 : 7-dimethylnaphthalene.³⁸



Oxidation of acetyloleanolic acid with chromic acid gives ketoacetyloleanolic acid,³⁹ which has been shown to be an $\alpha\beta$ -unsaturated ketone.⁴⁰ β -Amyrin benzoate is likewise oxidised to an $\alpha\beta$ -unsaturated ketone, β -amyrenonyl benzoate, formed by the oxidation of a methylene group immediately adjacent to the ethylenic linkage to a carbonyl group.⁴¹ Catalytic reduction of β -amyrenonyl benzoate led to complete reduction of the carbonyl group, the ethenoid linkage being unaffected, with formation of β -amyrin benzoate. Reduction of β -amyrenonol with sodium and alcohol, followed by treatment with acetic anhydride, has led to valuable information concerning the environment of the ethylenic linkage of β -amyrin. The product, β -amyradienol-I (as acetate), presumably formed by reduction of the carbonyl group of β -amyrenonol to a secondary alcohol and dehydration of the latter, contains a conjugated system of two ethylenic linkages. The absorption spectrum of β -amyradienol-I shows that this conjugated system is located in a single ring system. This series of changes shows that β -amyrin contains the unsaturated system (XIII), β -amyrenonol being (XIV) and β -amyradienol-I (XV).⁴²



The nature of the unsaturated centre in β -amyrin was further defined by C. W. Picard, K. S. Sharples, and F. S. Spring,⁴³ who have shown that

³⁸ L. Ruzicka, F. C. van der Sluys-Veer, and S. L. Cohen, *Helv. Chim. Acta*, 1939, **22**, 330.

³⁹ Z. Kitasato, *Acta phytochim.*, 1933, **7**, 183.

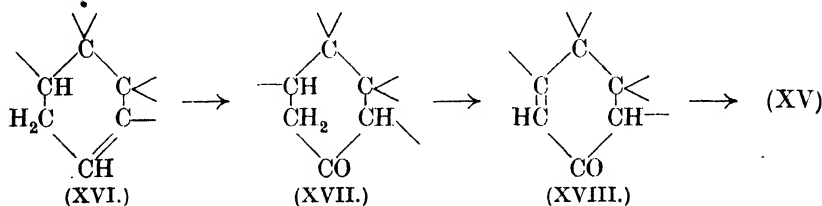
⁴⁰ L. Ruzicka and S. L. Cohen, *Helv. Chim. Acta*, 1937, **20**, 804.

⁴¹ J. H. Beynon, K. S. Sharples, and F. S. Spring, *J.*, 1938, 1233; L. Ruzicka, G. Müller, and H. Schellenberg, *Helv. Chim. Acta*, 1939, **22**, 758; J. C. E. Simpson, *J.*, 1940, 230; C. W. Picard and F. S. Spring, *ibid.*, p. 1198.

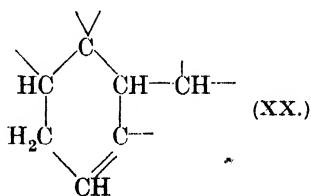
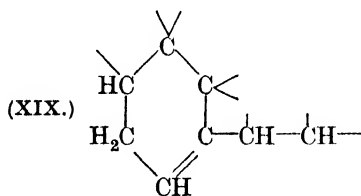
⁴² C. W. Picard and F. S. Spring, *J.*, 1940, 1198.

⁴³ *J.*, 1939, 1045.

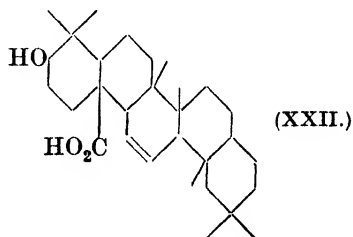
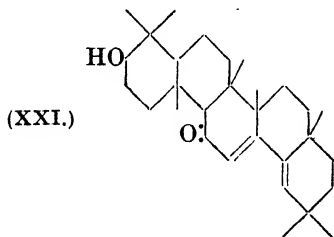
the so-called " β -amyrin oxide," obtained (as acetate) by oxidation of β -amyrin acetate with hydrogen peroxide,⁴⁴ or with perbenzoic acid⁴⁵ or with chromic anhydride,⁴¹ is a saturated keto-alcohol, β -amyranonol. Bromination of β -amyranonol acetate gives an $\alpha\beta$ -unsaturated ketone, *iso*- β -amyrenonol acetate, reduction of which with sodium and alcohol, followed by treatment with acetic anhydride, gives β -amyradienol-I (as acetate). The unsaturated system of β -amyrin can therefore be expanded to (XVI), β -amyranonol being (XVII) and *iso*- β -amyrenonol (XVIII).



A further elaboration of the unsaturated centre of β -amyrin has been made by C. W. Picard and F. S. Spring,⁴⁶ who have shown that β -amyrenonol esters are partially dehydrogenated when treated with bromine to yield the corresponding esters of β -amyradienonol, in which the presence of the grouping $-\text{CO}-\text{C}=\text{C}-\text{C}=\text{C}-$ has been spectroscopically established; from this it follows that the β -amyrin group of triterpenes contains the unsaturated fragment (XIX) or (XX); fragment (XIX) is included in both of the



hypothetical triterpene formulæ (III) and (IV), according to which β -amyradienonol will be (XXI).



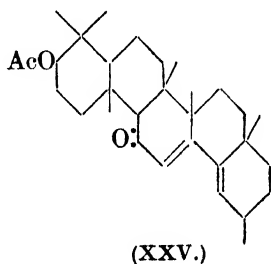
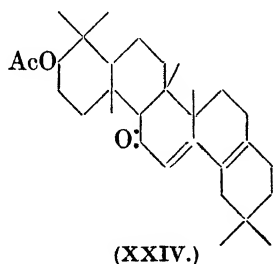
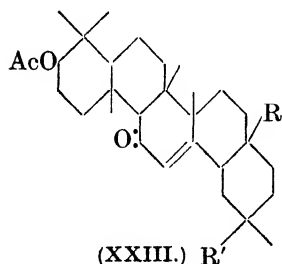
The relative positions of the double bond and the carboxyl group in oleanolic acid are determined by several requirements. First, the two must be so placed that lactonisation is possible under a variety of con-

⁴⁴ F. S. Spring, *J.*, 1933, 1345.

⁴⁵ F. S. Spring and T. Vickerstaff, *J.*, 1934, 1859.

⁴⁶ *J.*, 1941, 35.

ditions. The location of the double bond at $C_{10}:C_{11}$ and the carboxyl group attached to C_{13} (II) was proposed by L. Ruzicka; it is clearly inadequate, as it does not contain the unsaturated grouping (XIX) or (XX). The combination of ethenoid linkage at $C_{10}:C_{11}$ and carboxyl attached to C_{14} ⁴⁷ proved inadequate in that it did not account for the formation of 2:7-dimethylnaphthalene from the monomethyl ester of *isoleanolic* lactone dicarboxylic acid (see p. 194). Z. Kitasato⁴⁸ suggested structure (XXII) to explain the formation of certain oxidation products of oleanolic acid; the main feature of this investigation was a proof that the carboxyl group of oleanolic acid must be attached to an angular carbon atom common to rings A and B. Apart from the fact that this structure fails to interpret the formation of the characteristic oxidation products of the β -amyrin group [it does not contain either of the groupings (XIX) or (XX)], the interpretation of the experimental evidence upon which it rested has been shown to be incorrect.⁴⁹ A combination of the ethylenic linkage at $C_{12}:C_{13}$ and the carboxyl group attached to C_9 would lead to difficulties in considering the products of dehydrogenation; such a structure is, moreover, excluded by the conversion of oleanolic acid into nor- β -amyradienonol (below). The structures (III, $R = CO_2H$) and (IV, $R = CO_2H$), in which the double bond is located at $C_{12}:C_{13}$ and the carboxyl group attached to C_{17} and C_{20} respectively, give a satisfactory interpretation of the behaviour of oleanolic acid and related substances. Moreover, they include the fragment (XIX). Recently⁵⁰ a remarkable behaviour of ketoacetyl-oleanolic acid on heating with quinoline has been shown to be interpreted by structure (III, $R = CO_2H$) for oleanolic acid; the reaction is also adequately accounted for by means of structure (IV; $R = CO_2H$). The keto-acid loses the elements of formic acid and gives an acetoxy-dienone (the acetate of nor- β -amyradienonol) in which the presence of the grouping $-CO-C=C-C=C-$ has been spectroscopically demonstrated. According to structure (III; $R = CO_2H$) for oleanolic acid, ketoacetyloleanolic acid



will be (XXIII; $R = CO_2H$, $R' = Me$) and the acetoxy-dienone (XXIV), and according to structure (IV, $R = CO_2H$) for oleanolic acid, ketoacetyl-

⁴⁷ C. W. Picard, K. S. Sharples, and F. S. Spring, *J. Soc. Chem. Ind.*, 1939, **58**, 58.

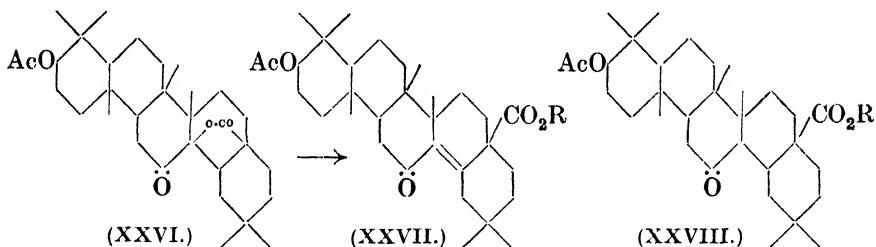
⁴⁸ *Acta phytochim.*, 1937, **10**, 199.

⁴⁹ L. Ruzicka and F. C. van der Sluys-Veer, *Helv. Chim. Acta*, 1938, **21**, 1371.

⁵⁰ L. Ruzicka, S. L. Cohen, M. Furter, and F. C. van der Sluys-Veer, *ibid.*, p. 1735.

oleanolic acid will be (XXIII; $R = \text{Me}$, $R' = \text{CO}_2\text{H}$) and the acetoxy-dienone (XXV).

L. Ruzicka, S. L. Cohen, M. Furter, and F. C. van der Sluys-Veer⁵⁰ have also shown that the conversion of ketoacetyloleanolic lactone (XXVI) into the $\alpha\beta$ -unsaturated ketone, *isoketoacetyloleanolic acid* (XXVII; $R = \text{H}$), is adequately interpreted in terms of formula (III; $R = \text{CO}_2\text{H}$) for oleanolic acid. Treatment of the *iso*-acid (XXVII; $R = \text{H}$) with quinoline gives a saturated ketoacetyl lactone; although this substance has the same crystalline form and approximately the same melting point as ketoacetyloleanolic lactone (XXVI), the authors do not consider the question of identity. Methyl *isoketoacetyloleanolate* (XXVII; $R = \text{Me}$) has been obtained by C. W. Picard and F. S. Spring⁵¹ by the bromination of the saturated methyl ketoacetyldihydro-oleanolate (XXVIII; $R = \text{Me}$). The last reaction is to be compared with the bromination of the acetyl derivative of β -amyranol (XXIX), to give *iso*- β -amyrenol, formulated as (XXX) in view of its conversion into β -amyradienol-I (XXXI); the difference in location of the $\alpha\beta$ -unsaturated ketonic system in (XXVII) and (XXX) may be real and attributable to the difference in the direction of enolisation of β -amyranol and the keto-ester (XXIX); on the other hand, it is conceivable that *iso*- β -amyrenol is (XXXII).



The structure (IV; $R = \text{CO}_2\text{H}$) for oleanolic acid gives a satisfactory interpretation of the reactions described with the exception that the ready formation of lactones from oleanolic acid, *e.g.*, of ketoacetyloleanolic lactone, which would be (XXXIII), appears to offer some difficulty; P. Bilham and G. A. R. Kon,³⁰ however, consider that such a structure is by no means excluded provided that rings D and E be *cis*-fused.

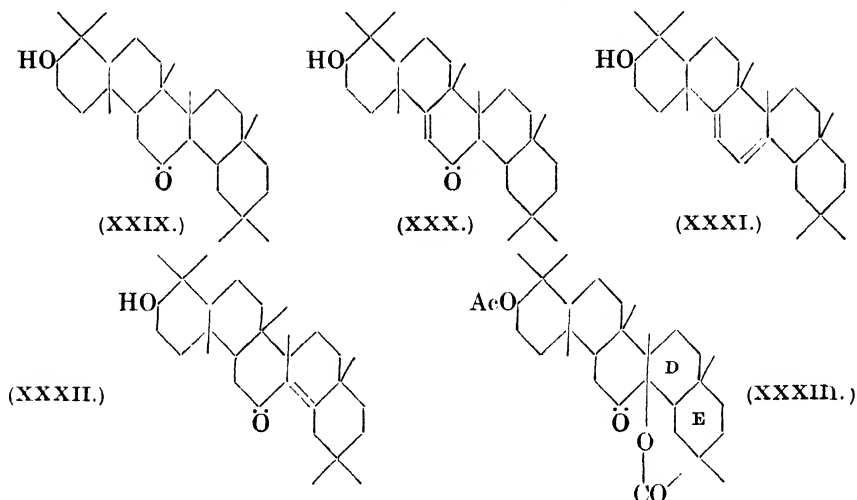
Before this section is concluded, mention must be made of the characteristic behaviour of members of this group when heated under controlled conditions with sulphur; dehydro-thio-derivatives are thereby obtained which give rise to well-defined oxidation products;⁵² this series of products has not been sufficiently characterised to warrant a detailed discussion at this stage.

Glycyrrhetic acid. Glycyrrhetic acid (Ig) has been shown to contain

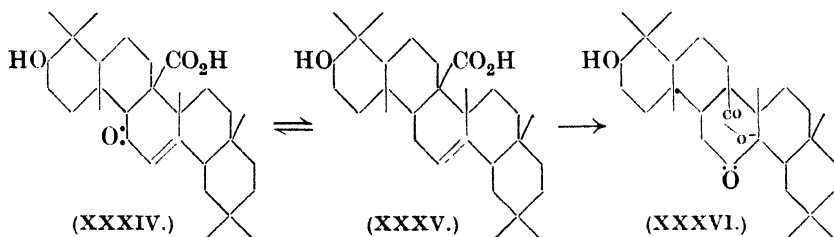
⁵¹ J., 1939, 1045.

⁵² W. A. Jacobs and E. E. Fleck, *J. Biol. Chem.*, 1930, **88**, 137, 153; 1932, **96**, 341; J. C. E. Simpson, *J.*, 1938, 1313; 1939, 755; C. W. Picard and F. S. Spring, *J.*, 1941, 35.

an $\alpha\beta$ -unsaturated ketone grouping; ⁵³ catalytic reduction of glycyrrhetic acid leads to the replacement of the carbonyl group by methylene with



formation of deoxoglycyrrhetic acid.⁵⁴ Deoxoglycyrrhetic acid is different from but isomeric with oleanolic acid. Since replacement of the carboxyl group of the deoxo-acid by methyl yields β -amyrin,⁵⁵ oleanolic acid and deoxoglycyrrhetic acid can only differ in the location of the carboxyl group. Information pertaining to the location of the carboxyl group of deoxoglycyrrhetic acid was obtained from a study of the oxidation of the acetyl derivative of this acid,⁵⁵ a mixture of acetyl glycyrrhetic acid and a ketolactone (as acetate) being obtained. The formation of these two products is completely analogous to that of ketoacetyloleanolic acid (XXXIII; $R = CO_2H$, $R' = CH_3$) and ketoacetyloleanolic lactone (XXVI) from acetyloleanolic acid. The carboxyl group of deoxoglycyrrhetic acid must therefore be in such a position with respect to the unsaturated centre that lactonisation is possible; a provisional formulation for glycyrrhetic acid (XXXIV) and deoxoglycyrrhetic acid (XXXV) has been suggested, according to which the ketolactone will be (XXXVI).

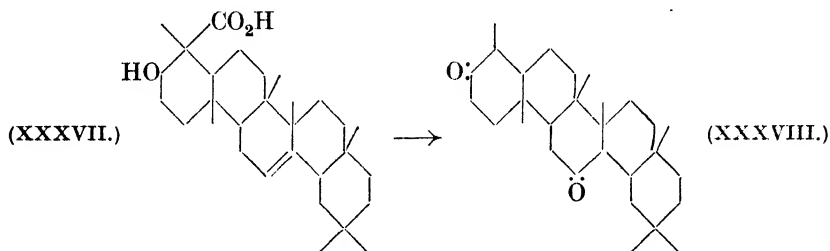


⁵³ L. Ruzicka and S. L. Cohen, *Helv. Chim. Acta*, 1937, **20**, 804.

⁵⁴ L. Ruzicka, H. Leuenberger, and H. Schellenberg, *ibid.*, 1937, **20**, 1271.

⁵⁵ L. Ruzicka and A. Marxer, *ibid.*, 1939, **22**, 196.

α-Boswellic acid. This isomer of oleanolic acid has been converted into *β*-amyrin and *epi-β*-amyrin by replacement of the carboxyl group by methyl.^{22, 23} Oxidation of *α*-boswellic acid (XXXVII) with chromic acid gives a diketone, $C_{29}H_{46}O_2$ (probably XXXVIII), formed by loss of carbon dioxide from an intermediate *β*-keto-acid with simultaneous oxidation of the ethylenic linkage to a carbonyl group.²² The structure of this degradation product has been confirmed by L. Ruzicka and A. Marxer,⁵⁶ who obtained the same diketone from hederagenin.



Echinocystic and quillaic acids. Hydrolysis of the saponin from *Echinocystis fabacea* gives the sapogenin, echinocystic acid,⁵⁷ $C_{30}H_{48}O_4$. This monobasic acid contains one ethylenic linkage and two secondary hydroxyl groups, one of which is in the *β*-position to the carboxyl group. The close proximity of the ethylenic linkage and the carboxyl group follows from the formation of a saturated bromo-lactone.⁵⁸ Oxidation of methyl echinocystate with chromic acid gives a diketo-methyl ester (XL), hydrolysis of which yields norechinocystendione (XLI) with loss of carbon dioxide. Clemmensen reduction of the diketo-methyl ester yields a monoketo-methyl ester (XLII), hydrolysis of which gives norechinocystenone (XLIII), again with loss of carbon dioxide. It was shown by D. Todd, G. H. Harris, and C. R. Noller⁵⁹ that Clemmensen reduction of either norechinocystenone or norechinocystendione gives the hydrocarbon oleanene III, identical with that obtained from oleanolic acid.⁶⁰ These results, together with the results of dehydrogenation of the acid,⁶¹ suggest that echinocystic acid is a hydroxyoleanolic acid in which the second (secondary) hydroxyl group is in the *β*-position to the carboxyl.

Quillaic acid, the sapogenin of quillaia bark, has recently been investigated by G. A. R. Kon and co-workers. It has been shown to have the formula $C_{30}H_{46}O_5$ and to be unsaturated. It is a monocarboxylic acid, the carboxyl group being in a "protected" position; it contains one aldehyde and two hydroxyl groups. The two hydroxyl groups are in *β*-positions, one with respect to the aldehyde group and the other to the

⁵⁶ *Helv. Chim. Acta*, 1940, **23**, 144.

⁵⁷ I. Bergsteinsson and C. R. Noller, *J. Amer. Chem. Soc.*, 1934, **56**, 1403.

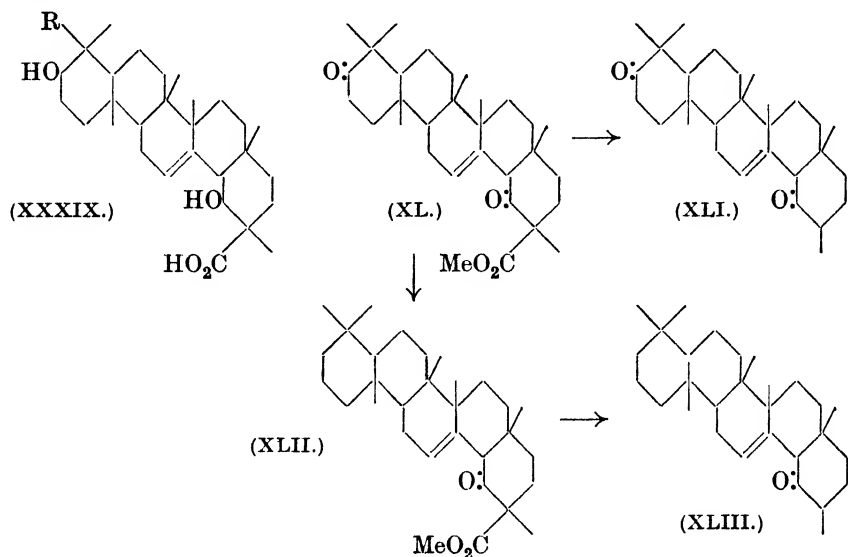
⁵⁸ W. R. White and C. R. Noller, *ibid.*, 1939, **61**, 983.

⁵⁹ *Ibid.*, 1940, **62**, 1624.

⁶⁰ *Annalen*, 1933, **502**, 223.

⁶¹ C. R. Noller, *J. Amer. Chem. Soc.*, 1934, **56**, 1582.

carboxyl group.⁶² P. Bilham and G. A. R. Kon⁶³ have shown that replacement of the aldehyde group in quillaic acid by methyl gives echinocystic



acid. If the structure of oleanolic acid is (IV; $R = CO_2H$), echinocystic acid must be either 19- (XXXIX; $R = CH_3$) or 21-hydroxyoleanolic acid, and quillaic acid the corresponding 19- (XXXIX; $R = CHO$) or 21-hydroxygypsogenin. Bilham and Kon conclude that the hydroxyl which is in the β -position to the carboxyl group in both echinocystic and quillaic acids must also be immediately adjacent to the junction of two rings, since they find that hydrolysis of the monoketo-ester (XLII) gives a mixture of two isomeric norechinocystenones (XLIII), which are considered to be stereoisomers differing in the mode of locking of rings D and E. Reduction (Kishner-Wolff) of each of the ketones (XLIII) gives the same hydrocarbon (*trans*-oleanene II); this is isomeric with oleanene II (*cis*) obtained by A. Winterstein and G. Stein⁶⁰ from oleanolic acid by decarboxylation and replacement of the hydroxyl group by hydrogen. Both *cis*- and *trans*-oleanene II are isomerised in acid media to give the same oleanene III. Bilham and Kon formulate these changes as shown on the following page.

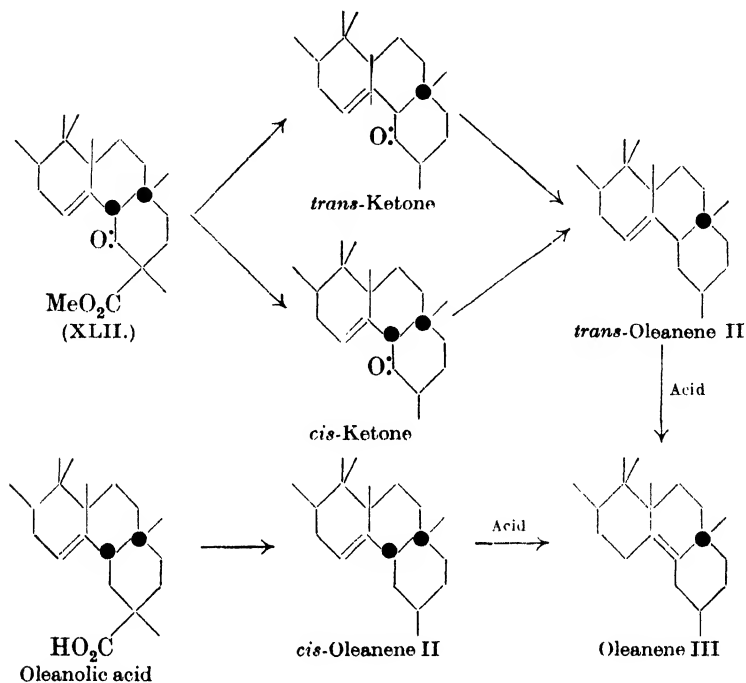
III. Lupeol Group.—*Lupeol and betulin.* Betulin, a monoethenoid, dihydric alcohol containing one primary and one secondary hydroxyl group, has been converted into lupeol by the replacement of the primary alcohol group ($CH_2 \cdot OH$) by methyl. Lupeol, $C_{30}H_{50}O$, contains one ethylenic linkage, since it readily absorbs one mole of hydrogen to give a saturated dihydro-derivative⁶⁴ and reacts with perbenzoic acid to give a monoxide;

⁶² D. F. Elliott and G. A. R. Kon, *J.*, 1939, 1130; D. F. Elliott, G. A. R. Kon, and H. R. Soper, *J.*, 1940, 612.

⁶³ *J.*, 1940, 1469; 1941, 552.

⁶⁴ L. Ruzicka, H. W. Huyser, M. Pfeiffer, and C. F. Seidel, *Annalen*, 1929, 471, 21.

lupeol is therefore pentacyclic. I. M. Heilbron, T. Kennedy, and F. S. Spring⁶⁵ found that ozonolysis of lupenyl acetate yielded formaldehyde



and concluded that the unsaturated centre was present as an exocyclic methylene group. The nature of this centre was further elucidated by L. Ruzicka and G. Rosenkranz,⁶⁶ who showed that oxidation of lupeol with permonophthalic acid yields an oxide which is readily isomerised to the saturated aldehyde, lupanalol,^{66, 67, 68} again showing that the unsaturated centre is present as $=CH_2$. Oxidation of lupeol with selenium dioxide gives an $\alpha\beta$ -unsaturated aldehyde, lupenalol, reduction of which by the Kishner-Wolff method regenerates lupeol. L. Ruzicka and G. Rosenkranz⁶⁸ conclude that lupeol contains an *isopropenyl* group (XLIV) and that lupenalol is (XLV).

Among the products of ozonolysis of lupenyl acetate is the acetate of a hydroxy-acid,⁶⁹ which is also obtained by oxidation of lupenalol (as acetate) with chromic acid.⁶⁸ The formula of this hydroxy-acid was shown to be $C_{28}H_{46}O_3$ by the determination of the equivalent of the corresponding hydroxyl-free acid; it is therefore formulated as a bisnorlupanolic acid (XLVI). Further confirmation of the presence of an *isopropenyl* group

⁶⁵ *J.*, 1938, 329.

⁶⁶ *Helv. Chim. Acta*, 1939, **22**, 778.

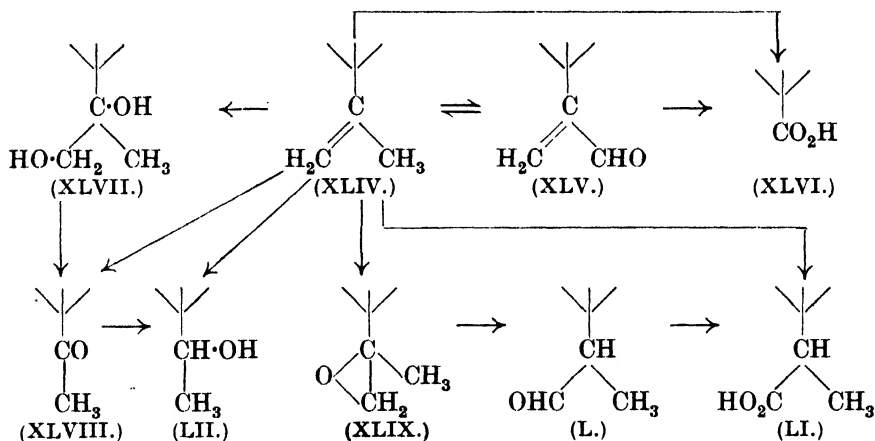
⁶⁷ E. R. H. Jones and R. J. Meakins, *J.*, 1940, 1335.

⁶⁸ L. Ruzicka and G. Rosenkranz, *Helv. Chim. Acta*, 1940, **23**, 1311.

⁶⁹ A. Duerden, I. M. Heilbron, W. McMeeking, and F. S. Spring, *J.*, 1939, 322.

in lupeol is obtained in an observation of H. Dieterle and A. Salomon⁷⁰ that oxidation of lupeol (as acetate) with chromic anhydride gives acetone. Oxidation of lupenyl acetate with either chromic acid or ozone yields a neutral keto-alcohol,⁷¹ m. p. 232°, which has been shown by E. R. H. Jones and R. J. Meakins⁷² to have the structure (XLVIII); these authors find that oxidation of lupeol with osmium tetroxide yields lupanetriol, which forms a diacetate only, thus indicating the tertiary nature of one of the introduced hydroxyl groups. Oxidation of lupanetriol (XLVII) with lead tetra-acetate gives the keto-alcohol (XLVIII), norlupananol, m. p. 232°.

Oxidation of lupenyl acetate with chromic acid gives the corresponding ester of a saturated acetoxy-monocarboxylic acid $C_{32}H_{50}O_4$, acetyl-lupanolic acid.⁷³ An isomeric acetylislupanolic acid is obtained by the oxidation of lupenyl acetate oxide (XLIX) and of lupanallyl acetate (L).⁶⁶ The different methyl esters of the two isomeric lupanolic acids are hydrolysed by concentrated alkali solution to the same lupanolic acid. The nature of the difference between acetyl-lupanolic acid (LI) and acetylislupanolic acid is not established; according to L. Ruzicka and M. Brenner⁷⁴ they may be stereoisomers differing in orientation around the carboxyl-carrying carbon atom.



The behaviour of betulin (and of its diacetate) on oxidation has been shown to be very similar to that of lupeol. Thus with osmic acid betulin gives a saturated tetrol (XLVII), which with periodic acid gives a dihydroxy-ketone $C_{29}H_{48}O_3$, norlupanondiol (XLVIII). Again, oxidation of betulin

⁷⁰ *Arch. Pharm.*, 1932, **270**, 540.

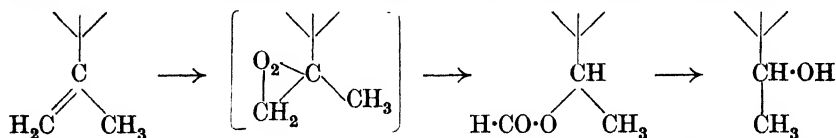
⁷¹ I. M. Heilbron, T. Kennedy, and F. S. Spring, *J.*, 1938, 329; A. Duerden, I. M. Heilbron, W. McMeeking, and F. S. Spring, *J.*, 1939, 222; L. Ruzicka, H. Schellenberg, and G. Rosenkranz, *Helv. Chim. Acta*, 1938, **21**, 1391; F. Biedebach, *Arch. Pharm.* 1939, **277**, 163.

⁷² *J.*, 1940, 456.

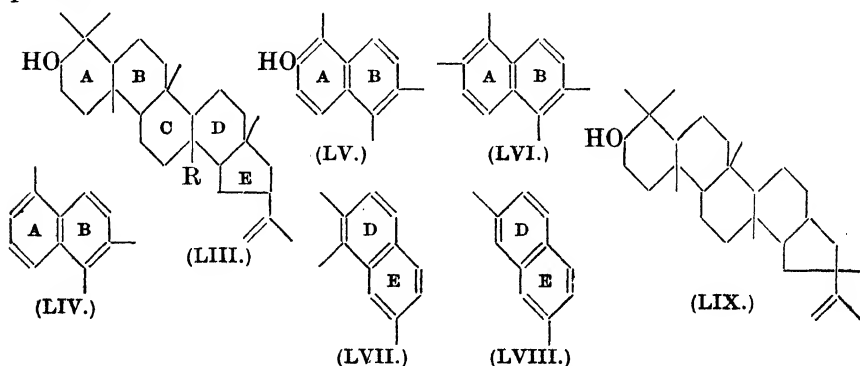
⁷³ A. Duerden, I. M. Heilbron, W. McMeeking, and F. S. Spring, *J.*, 1939, 222; J. Ruzicka and G. Rosenkranz, *Helv. Chim. Acta*, 1938, **21**, 1391; 1940, **23**, 1311.

diacetate gives the diacetate of norlupanondiol (XLVIII) and a mixture of two isomeric diacetoxyilupanic acids (LI).⁷⁴

Finally, the behaviour of lupeol and betulin towards hydrogen peroxide may be mentioned. In the case of lupeol, I. M. Heilbron, T. Kennedy, and F. S. Spring⁶⁵ found that a saturated diol was obtained which was identical with the reduction product (LII) of the keto-alcohol subsequently shown to be norlupanonol (XLVIII). The mechanism of this reaction has been established by L. Ruzicka and M. Brenner,⁷⁴ who find that oxidation of betulin diacetate by hydrogen peroxide gives a diacetate-formate of norlupantriol; the triol is identical with the reduction product of norlupanondiol (XLVIII) and its formation may be formulated as follows:



The establishment of the presence of an *isopropenyl* group in lupeol and in betulin shows that these triterpenes cannot possess the hydrocypicene structure which has been postulated for the β -amyrin group. A hypothetical formula (LIII) has been advanced by L. Ruzicka and G. Rosenkranz,⁶⁸ based upon the experimental results described above and upon the nature of the products of dehydrogenation. When dehydrogenated with selenium, lupeol gives 1:2:5-trimethylnaphthalene (LIV), 6-hydroxy-1:2:5-trimethylnaphthalene (LV), and possibly 1:2:5:6-tetramethylnaphthalene (LVI), and betulin gives 6-hydroxy-1:2:5-trimethylnaphthalene (LV), 1:2:5:6-tetramethylnaphthalene (LVI), 1:2:7-trimethyl-(LVII) and 2:7-dimethyl (LVIII)-naphthalenes and 1:8-dimethylpicene.*



During dehydrogenation it is assumed that the group R ($\text{CH}_2\cdot\text{OH}$) in betulin migrates to C_{14} , a change which, together with simultaneous ring E

⁷⁴ *Helv. Chim. Acta*, 1940, **23**, 1325.

* The formation of dimethylpicene is in doubt, since L. Ruzicka and G. Rosenkranz⁶⁹ mention that this hydrocarbon was only isolated once in a case where a large amount of impure betulin was used.

enlargement, would account for the formation of the "normal" dehydrogenation products from rings D and E [(LVII) and (LVIII)]. The non-formation of these hydrocarbons from lupeol is explained by the inability of the unsubstituted $R(CH_3)$ group to migrate; hitherto no dehydrogenation product ascribable to rings D and E has been isolated from lupeol.

E. R. H. Jones and R. J. Meakins⁷⁵ observe that the non-reactivity of the carbonyl and carboxyl groups in norlupanonol (XLVIII) and bis-norlupanolic acid (XLVI) is not compatible with the lupeol structure (LIII); they suggest that the isopropenyl group is attached to a quaternary carbon atom as in (LIX).

F. S. S.

7. NATURAL QUINONE PIGMENTS.

The recent report on natural naphthaquinone pigments¹ makes it desirable that a review be made at this stage of all the natural quinones. These substances have not hitherto been reported upon as a group, although occasional reference to individual members has been made in earlier Reports, and the chemistry of the anthraquinone derivatives obtained from insects has been discussed in the Reports for 1913 and 1916. Work on natural quinones has been spread fairly evenly over many years, but interest in the group has recently quickened in view of the biological properties of vitamin K and of the echinochromes and the probability that other members are also concerned in oxidation-reduction processes in living matter. The number of quinone pigments known to occur naturally is large and there is every reason to expect that the number will be still further increased as work on fungi and lichens is extended. They are found in both higher and lower plants and in the animal kingdom, and it is of interest to note that anthraquinone (hœlite) and a hexahydroxyanthraquinone (græbeite) have been found in a soft shale.² In this review the pigments are classified as derivatives of benzoquinone, naphthaquinone, phenanthraquinone and anthraquinone.

Benzoquinone Derivatives.

Of the small group of naturally occurring benzoquinone derivatives the simplest are 2 : 6-dimethoxybenzoquinone (I) from *Adonis vernalis*³ and the mould pigment fumigatin, produced by one strain of *Aspergillus fumigatus* Fresenius,⁴ which has been proved by synthesis to be 3-hydroxy-4-methoxytoluquinone (II; $R = H$).⁵ Spinulosin, first isolated from *Penicillium spinulosum* Thom., was shown to be (II; $R = OH$),⁴ and the structure has been verified by synthesis.⁶ Spinulosin can readily be prepared from fumigatin in the laboratory,⁴ and its occurrence in another strain of *A. fumigatus*⁷

⁷⁵ J., 1941, 761.

¹ Ann. Reports, 1939, **36**, 278.

² A. Treibs and H. Steinmetz, *Annalen*, 1933, **506**, 171.

³ W. Karrer, *Helv. Chim. Acta*, 1930, **13**, 1454.

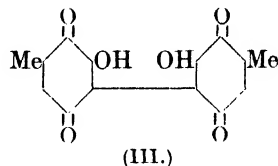
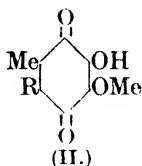
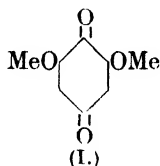
⁴ W. K. Anslow and H. Raistrick, *Biochem. J.*, 1938, **32**, 687.

⁵ W. Baker and H. Raistrick, *J.*, 1941, 670.

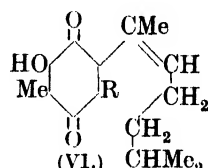
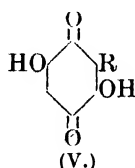
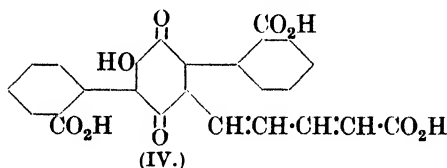
⁶ W. K. Anslow and H. Raistrick, *Biochem. J.*, 1938, **32**, 803.

⁷ *Idem, ibid.*, p. 2288.

is of some biological interest. Closely related to these simple toluquinone derivatives is phœnicin, the red pigment of *Penicillium phœniceum* van Beyma and of *P. rubrum* Grasberger-Stoll. Its formulation as 2:2'-dihydroxy-4:4'-dimethyldibenzoquinone (III) was arrived at by degradation and confirmed by synthesis from 4:4'-ditoluquinone, which was subjected to Thiele acetylation, followed by hydrolysis and oxidation of the leuco-phœnicin thus produced.⁸



From members of the higher fungi three derivatives of 2:5-diphenylbenzoquinone have been isolated. Polyporic acid, from the shelf fungus *Polyporus nidulans* Pers., and atromentin, from *Paxillus atrotomentosus* Batsch, are respectively 3:6-dihydroxy-2:5-diphenylbenzoquinone⁹ and 3:6-dihydroxy-2:5-di-(*p*-hydroxyphenyl)benzoquinone.¹⁰ The structures allotted by F. Kögl and his co-workers rest on the formation of *p*-terphenyl on distillation with zinc dust and of benzoic and *p*-hydroxybenzoic acids respectively on oxidation. Polyporic acid has been synthesised from phenyl-acetic ester and oxalic ester by the action of sodium in presence of atmospheric oxygen⁹ and an analogous synthesis has been used for atromentin.¹¹ This synthetic route, the mechanism of which is discussed by F. Kögl and A. Lang,¹² is less satisfactory in practice than the hydroxylation of the corresponding 2:5-diarylquinols.^{11, 13} Muscarufin, C₂₅H₁₆O₉, the orange-red pigment of the fly agaric *Amanita muscaria* L., has been investigated by F. Kögl and H. Erxleben.¹⁴ The main evidence on which the allotted structure (IV) rests may be briefly summarised. Muscarufin yields *p*-terphenyl on zinc dust distillation, and contains one hydroxyl group, three carboxyls and two conjugated ethenoid linkages. Saturation of the double bonds, followed by oxidation with hydrogen peroxide, yields adipic acid and *ca.* 1.4 mols. of phthalic acid.



⁸ T. Posternak, *Helv. Chim. Acta*, 1938, **21**, 1326.

⁹ F. Kögl, *Annalen*, 1925, **447**, 78.

¹⁰ F. Kögl and J. Postowsky, *ibid.*, 1924, **440**, 19; 1925, **445**, 159; F. Kögl and H. Becker, *ibid.*, 1928, **465**, 211.

¹¹ F. Kögl, *ibid.*, 1928, **465**, 243.

¹² *Ber.*, 1926, **59**, 910.

¹³ P. R. Schildneck and R. Adams, *J. Amer. Chem. Soc.*, 1931, **53**, 2373.

¹⁴ *Annalen*, 1930, **479**, 11.

Embelin is a golden-yellow pigment from the fruits of *Embelia ribes* used in India as an anthelmintic. Its constitution as 3 : 6-dihydroxy-2-laurylbenzoquinone (V; $R = C_{12}H_{25}$) was until recently accepted on the basis that it gave no depression in m. p. when mixed with a synthetic specimen of (V; $R = C_{12}H_{25}$),¹⁵ although the formation of lauric acid on oxidation and of α -ketomyristic acid on boiling with alkali^{15, 16} were difficult to understand on this formula. The matter has now been cleared up by M. Asano and K. Yamaguti,¹⁷ who have shown that mixed m. p.'s are unreliable in this series and that embelin is actually 3 : 6-dihydroxy-2-undecylbenzoquinone (V; $R = C_{11}H_{23}$). The same authors¹⁸ have also shown that rapanone, the very similar pigment from *Rapanea Maximowiczii*, is the corresponding tridecyl compound (V; $R = C_{13}H_{27}$). Mæsaquinone, from the fruits of the related plant *Mæsa japonica*, is considered to have structure (V; $R = C_{20}H_{39}$).¹⁹ The side chain is believed to be normal and not branched, heneicosanoic acid being obtained on oxidising dihydromæsaquinone, but the location of the double bond is unknown. Related to these pigments is pedicinin, from *Didymocarpus pedicellata*, which on the basis of recent evidence is believed to be 3 : 6-dihydroxy-5-methoxy-2-cinnamoylbenzoquinone.²⁰

In various Mexican species of *Perezia* there occurs perezone (pipitzahoiic acid), a benzoquinone derivative of formula $C_{15}H_{20}O_3$, which has recently been investigated by F. Kögl and A. G. Boer.²¹ Perezone gives a violet anilino-derivative convertible by acids into hydroxyperezone, $C_{15}H_{20}O_4$, which, like the parent pigment, contains one ethenoid linkage. Oxidation of hydroxydihydroperezone yields α , ϵ -dimethylheptoic acid and ozonolysis of hydroxyperezone gives $\alpha\beta$ -diketobutyric acid. These facts lead to structure (VI; $R = H$) for perezone and (VI; $R = OH$) for hydroxyperezone. Perezone is of particular interest, as it may be regarded as a quinone of the sesquiterpene series. Concentrated sulphuric acid cyclises hydroxyperezone, the product, perezinone, being a derivative of cadalene.

Naphthaquinone Derivatives.¹

Following the structural elucidation and synthesis of vitamin K_1 an important publication by S. B. Binkley, R. W. McKee, S. A. Thayer, and E. A. Doisy²² has considerably clarified the structure of vitamin K_2 , the antihæmorrhagic substance found in decaying fish meal.²³ Ozonolysis of dihydrovitamin K_2 diacetate gave 1 : 4-diacetoxy-2-methylnaphthalene-3-acetaldehyde, identical with the aldehyde obtained by similar means from vitamin K_1 , accompanied by approximately 1 mol. of acetone and 5 mols. of

¹⁵ K. H. Hasan and E. Stedman, *J.*, 1931, 2112.

¹⁶ R. Kaul, A. C. Ray, and S. Dutt, *J. Indian Chem. Soc.*, 1931, **8**, 231; K. S. Nargund and B. W. Bhide, *ibid.*, p. 237.

¹⁷ *J. Pharm. Soc. Japan*, 1940, **60**, 34.

¹⁸ *Ibid.*, p. 237.

¹⁹ M. Hiramoto, *Proc. Imp. Acad. Tokyo*, 1939, **15**, 220.

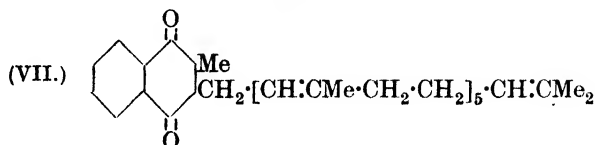
²⁰ P. K. Bose and P. Dutt, *J. Indian Chem. Soc.*, 1940, **17**, 499.

²¹ *Rec. Trav. chim.*, 1935, **54**, 779.

²² *J. Biol. Chem.*, 1940, **133**, 721.

²³ R. W. McKee, S. B. Binkley, D. W. McCorquodale, S. A. Thayer, and E. A. Doisy, *J. Amer. Chem. Soc.*, 1939, **61**, 1295; *J. Biol. Chem.*, 1939, **131**, 327.

lævulaldehyde. On the basis of this evidence and an empirical formula $C_{41}H_{56}O_2$, structure (VII) is suggested for vitamin K_2 .



The investigation of the naphthaquinone pigments present in sea urchin eggs has been continued by R. Kuhn and K. Wallenfels.²⁴ Although fully mature ovaries of *Arbacia pustulosa* yielded only echinochrome A (ethyl-pentahydroxy-1 : 4-naphthaquinone), it is now found that the ovaries of younger females collected at a different season yield in addition echinochrome B, also a hydroxylated naphthazarin derivative, and echinochrome C, whose nature is as yet unknown. All three pigments are present in the organism as prosthetic groups in relatively stable, non-dialysable, binary or ternary complexes where they are combined with substances of high molecular weight, probably protein in nature; these high molecular weight components exercise a remarkable effect on the chemical and biological properties of the pigments. Quite apart from the fact that the sea urchin products are the only naphthaquinones so far found among animal pigments, their function in the reproductive processes of *Arbacia* is of the greatest biological interest. Echinochrome A in the form of a high molecular weight complex is liberated in sea water by the eggs, where it renders the spermatozoa motile and enables fertilisation of the egg to occur. This effect is shown by echinochrome A itself,²⁵ which confers motility on *Arbacia* spermatozoa at the enormous dilution of 1.2×10^9 . The complex containing echinochrome A as prosthetic group, which is found in the watery secretion of intact eggs, is approximately 100 times more active than the free pigment. This function of echinochrome A is analogous to that of certain carotenoids in *Chlamydomonas* among the green algæ. Three new pigments of a similar type have been isolated from the spines of sea urchins, spinochrome-Aka, spinochrome-F and spinochrome-M.²⁶ Of these, the first named (from *Pseudocentrotus depressus*) is formulated as 2 : 3 : 5 : 7 : 8-pentahydroxy-6-methyl-1 : 4-naphthaquinone.

Phenanthraquinone Derivatives.

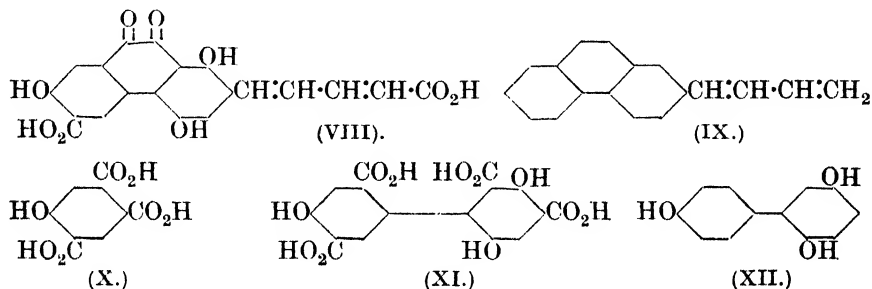
Up to the present only three quinones derived from phenanthrene have been isolated from plants, a fact which is perhaps surprising in view of the frequent occurrence of hydrophenanthrene derivatives among other classes of natural products. Thelephoric acid, the dark red quinone found in various brown heath fungi (*Thelephora* species), was the first member of the group to be thoroughly investigated. In a brilliant degradative investigation carried out with very small amounts of material F. Kögl, H. Erxleben,

²⁴ *Ber.*, 1940, **63**, 458.

²⁵ M. Hartmann, O. Schartau, R. Kuhn, and K. Wallenfels, *Naturwiss.*, 1939, **27**, 433.

²⁶ C. Kuroda and H. Ohshima, *Proc. Imp. Acad. Tokyo*, 1940, **16**, 214.

and L. Jänecke²⁷ showed it to be a 9 : 10-phenanthraquinone of structure (VIII). This structure accounts satisfactorily for the following facts. Zinc dust distillation of thelephoric acid yields α -2-phenanthrylbutadiene (IX), oxidisable to phenanthrene-2-carboxylic acid. Chromic acid oxidation of triacetyl thelephoric acid, followed by hydrolysis, yields hydroxytrimellitic acid (X) and a trihydroxydiphenyltetracarboxylic acid believed to be (XI), giving on decarboxylation 4 : 2' : 5'-trihydroxydiphenyl (XII), identified by synthesis. Oxidation of tetrahydrothlephoric acid with hydrogen peroxide yields (X) and adipic acid. The same unsaturated side chain is present in muscarufin and in thelephoric acid.



The remarkable green pigment xylindein, $C_{34}H_{26}O_{11}$, obtained from the fungus *Peziza æruginosa* P. found on decaying beech, oak, and birch wood known for over a century, has been obtained in a pure state by F. Kögl and his collaborators and submitted to a preliminary investigation.²⁸ Insufficient evidence is available to permit of a structural formula being advanced, but it evidently contains a phenanthrene nucleus, since this hydrocarbon is obtained from xylindein derivatives on zinc dust distillation. It is not, however, a 9 : 10-phenanthraquinone and it has been suggested that it may be derived from the unknown 2 : 7-phenanthraquinone.

The root of *Salvia miltiorrhiza*, used in China as a purgative under the name "tanshen," yields three related pigments, tanshinones I, II and III. Tanshinone I, $C_{18}H_{20}O_3$, gives on reductive acetylation a diacetate and is an *o*-quinone, since it forms a quinoxaline derivative with *o*-phenylenediamine.²⁹ Considerable progress in its structural elucidation has been made by F. v. Wessely and S. Wang.³⁰ Oxidation with chromic acid or hydrogen peroxide gives as main product an acid anhydride, $C_{13}H_8O_3$, whose parent acid furnishes 1-methylnaphthalene on decarboxylation. The product $C_{13}H_8O_3$ was identified by synthesis as 1-methylnaphthalene-5 : 6-dicarboxylic acid anhydride (XIII), the structure of the major part of the tanshinone I molecule thereby being fixed.

Since two oxygen atoms are present in an *o*-quinonoid system, a third

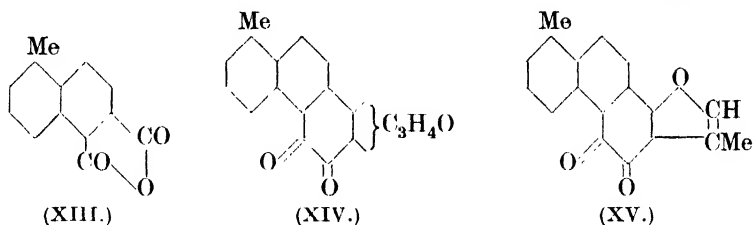
²⁷ *Annalen*, 1930, **482**, 170.

²⁸ F. Kögl and G. v. Tœuffenbach, *Annalen*, 1925, **445**, 170; F. Kögl and H. Erxleben, *ibid.*, 1930, **484**, 65.

²⁰ M. Nakao and T. Fukushima, *J. Pharm. Soc. Japan*, 1934, **54**, 154.

³⁰ *Ber.*, 1940, 73, 19.

six-membered ring must be fused to the naphthalene nucleus of (XIII) in the 5 : 6-position. This leads to three partial formulæ for the pigment, of



which (XIV) represents one, the other two differing only in the location of the quinone grouping in the third ring. The remaining oxygen could not be characterised and is therefore believed to be present in an ether linkage. Furthermore, tanshinone I contains two side-chain methyl groups, one of which is already accounted for in product (XIII); the remaining one must therefore be present in the group C_3H_4O . As the pigment contains no aliphatic double bonds, it is reasonably concluded that the group C_3H_4O must be part of a furan ring fused to the third ring in the molecule, *i.e.*, that tanshinone I is a phenanthrafuran derivative.³⁰ Of the four possible structures for the pigment on this hypothesis, (XV), derived from the partial formula (XIV), seems the most attractive in view of the resemblance between its carbon skeleton and that of typical diterpene derivatives.

Anthraquinone Derivatives.

Anthraquinone derivatives form by far the largest group of natural quinone pigments and occur in higher plants, fungi, lichens and in insects. Although the constitution of all members has not been elucidated, about fifty representatives are known, and only a very brief survey of them can be made here. For convenience the pigments will be dealt with according to their source.

Higher Plants.—In higher plants anthraquinones occur both in the free state and as glycosides. Many have been known for a long time and plants containing them have for centuries found application in dyeing (*e.g.*, madder) and in medicine (*e.g.*, senna, aloes). As much of the work on them is not of very recent date and since comprehensive surveys of the field at various stages are available,³¹ the position up to about ten years ago may be summarised very briefly. Anthraquinone derivatives have been found in plants belonging to several families, where they occur variously in roots, wood, bark and leaves. A survey of the literature reveals that they are all polyhydroxy-compounds which may be regarded as derivatives either of anthraquinone itself or of 2-methylantraquinone, and that they fall into two distinct groups according to their origin.

³¹ A. G. Perkin and A. E. Everest: "The Natural Organic Colouring Matters," London, 1918; L. Rosenthaler, "Anthracenglucoside" in G. Klein, "Handbuch der Pflanzenanalyse," Vol. III, Vienna, 1932; R. Eder and B. Siegfried, *Pharm. Acta Helv.*, 1939, 14, 34.

Group I, obtained from *Rubiaceæ*: 2-Hydroxyanthraquinone, alizarin and its 1-methyl ether, hystazarin monomethyl ether, purpuroxanthin, purpurin, anthragallol 1:2- and 1:3-dimethyl ethers, rubiadin (1:3-dihydroxy-2-methylantraquinone), munjistin (1:3-dihydroxyanthraquinone-2-carboxylic acid), 5:7-dihydroxy-2-methylantraquinone, ψ -purpurin (1:2:4-trihydroxyanthraquinone-3-carboxylic acid), and morindone (1:5:6-trihydroxy-2-methylantraquinone) with its monomethyl ether.

Group II, obtained from *Polygonaceæ*, *Rhamnaceæ*, *Leguminosæ*, and *Liliaceæ*: Chrysophanol (4:5-dihydroxy-2-methylantraquinone), rhein (4:5-dihydroxyanthraquinone-2-carboxylic acid), emodin (4:5:7-trihydroxy-2-methylantraquinone) and its 7-methyl ether physcion, aloe-emodin (4:5-dihydroxy-2-hydroxymethylantraquinone), natalæ-emodin (3:6-dihydroxy-2-methylantraquinone), and methyl natalæ-emodin (3:6-dihydroxy-2-methoxymethylantraquinone).

It should be emphasised that the above list omits a number of compounds in each group which are poorly characterised or of uncertain constitution. In individual plants it is usual to find several members of the appropriate group, and particularly in the case of plants yielding Group II the corresponding anthranols frequently occur simultaneously either free or as glycosides. In recent years there has been less activity in this field, although the isolation of 2-methylantraquinone from teak wood³² and the synthesis of rubiadin 3- β -*D*-glucoside, occurring in madder,³³ have been reported. Ruberythric acid from madder is now believed to be alizarin 2- β -primeveroside.³⁴

Fungi.—Among the higher fungi several *Boletus* species yield a bright red pigment, boletol, which has been investigated by F. Kögl and W. B. Deijs.³⁵ Boletol was shown by degradative methods to be 1:2:4-trihydroxyanthraquinone-5 or 8-carboxylic acid; it has been synthesised, but the method employed still leaves the location of the carboxyl group uncertain. Boletol is exceptional among the plant anthraquinones in being apparently derived from 1-methylantraquinone. The blood-red agaric *Dermocybe sanguinea* Wulff has been shown to contain emodin and dermocybin, the latter being a tetrahydroxymethoxy-2-methylantraquinone in which the orientation of the methoxyl and hydroxyl groups is uncertain.³⁶

In recent years a good deal of attention has been directed to the production of anthraquinone derivatives by lower fungi. From moulds belonging to the genus *Helminthosporium* responsible for leaf stripe diseases in cereals and grasses, four anthraquinone pigments, helminthosporin, catenarin, cynodontin and tritisporin, have been isolated. Helminthosporin, C₁₅H₁₀O₅, first isolated from the mycelium of *H. gramineum* Rabenhorst³⁷ and

³² K. Kafuku and K. Sebe, *Bull. Chem. Soc. Japan*, 1932, 7, 114.

³³ E. T. Jones and A. Robertson, *J.*, 1930, 1699.

³⁴ E. T. Jones and A. Robertson, *J.*, 1933, 1167; D. Richter, *J.*, 1936, 1701.

³⁵ *Annalen*, 1935, 515, 10, 23.

³⁶ F. Kögl and J. Postowsky, *Annalen*, 1925, 444, 1.

³⁷ J. H. V. Charles, H. Raistrick, R. Robinson, and A. R. Todd, *Biochem. J.*, 1933, 27, 499.

subsequently from *H. cynodontis* Marignoni,³⁸ *H. catenarium* Drechsler,³⁹ and *H. tritici-vulgaris* Nisikado,³⁹ was shown to contain three hydroxyl groups and to yield 2-methylantracene on distillation with zinc dust. The orientation of the hydroxyl groups was determined by oxidation of triacetylhelminthosporin with chromic acid, followed by hydrolysis to helminthosporic acid, $C_{15}H_8O_7$, which on decarboxylation gave 1 : 4 : 5-trihydroxyanthraquinone, identified by synthesis. The location of the 2-methyl group relative to the hydroxyls follows rigidly from the production of nitrococcusic acid (2 : 4 : 6-trinitro-5-hydroxy-*m*-toluic acid) on degradation of helminthosporin with nitric acid; helminthosporin must therefore be 4 : 5 : 8-trihydroxy-2-methylantraquinone.³⁷ This structure was confirmed by complete synthesis of the pigment.⁴⁰ Cynodontin, $C_{15}H_{10}O_6$, isolated from *H. cynodontis* Marignoni,³⁸ *H. euschlaenae* Zimmermann,³⁸ and *H. avenae* Eidam,³⁹ is identical with the product obtained on oxidising helminthosporin with manganese dioxide and concentrated sulphuric acid, and is therefore 1 : 4 : 5 : 8-tetrahydroxy-2-methylantraquinone.³⁸ This structure has recently been confirmed by a second unambiguous synthesis.⁴¹ Accompanying helminthosporin in *H. gramineum* Rabenhorst is a red pigment, $C_{15}H_{10}O_6$, at first called "hydroxyisohelminthosporin" ³⁷ and later renamed catenarin when it was found in larger amount in *H. catenarium* Drechsler; ³⁹ it has also been isolated from *H. velutinum* Link ³⁹ and from *H. tritici-vulgaris* Nisikado.³⁹ The structural elucidation of catenarin ^{39, 42} proved a matter of some difficulty, particularly as, although it yielded 2-methylantracene on zinc dust distillation, its tetra-acetate could not be oxidised in the side chain. Oxidation of catenarin tetramethyl ether, however, gave both 3 : 6-dimethoxy-4-methylphthalic anhydride and 3 : 5-dimethoxyphthalic anhydride, and this, coupled with other evidence, suggested that catenarin was 1 : 4 : 5 : 7-tetrahydroxy-2-methylantraquinone,⁴² a structure now confirmed by synthesis.⁴³ The constitution of tritisporin, $C_{15}H_{10}O_7$, from *H. tritici-vulgaris* Nisikado, is as yet uncertain, but the available evidence suggests that it may be 1 : 4 : 5 : 7-tetrahydroxy-2 or 3-hydroxymethylantraquinone.³⁹ The amount of colouring matter produced by some of the *Helminthosporia* is remarkable; e.g., in *H. gramineum* Rabenhorst grown on a Czapek-Dox glucose medium, the colouring matter amounts to some 30% of the dry weight of mycelium.³⁷

From *Penicillium* species, too, several anthraquinone derivatives have been isolated. *P. cyclopium* Westling yields ω -hydroxyemodin (4 : 5 : 7-trihydroxy-2-hydroxymethylantraquinone) and emodic acid (4 : 5 : 7-trihydroxyanthraquinone-2-carboxylic acid).⁴⁴ ω -Hydroxyemodin has been shown by direct comparison to be identical with the pigment from *P. citreoseum* Dierckx,⁴⁴ and its 7-methyl ether occurs in *P. roseo-purpureum*

³⁸ H. Raistrick, R. Robinson, and A. R. Todd, *Biochem. J.*, 1933, **27**, 1170.

³⁹ *Idem, ibid.*, 1934, **28**, 559.

⁴⁰ *Idem, J.*, 1933, 488.

⁴¹ W. K. Anslow and H. Raistrick, *Biochem. J.*, 1940, **34**, 1546.

⁴² *Idem, ibid.*, p. 1124.

⁴³ *Idem, ibid.*, 1941, **35**, 1006.

⁴⁴ W. K. Anslow, J. Breen, and H. Raistrick, *ibid.*, 1940, **34**, 159.

Dierckx.⁴⁵ Of less thoroughly investigated pigments from *Penicillia*, both carviolin, $C_{16}H_{12}O_6$, and carviolacin, $C_{20}H_{16}O_7$, from *P. carmino-violaceum* Biourge, appear to be derivatives of 2-methylantraquinone,⁴⁶ and funiculosin, $C_{15}H_{10}O_5$, from *P. funiculosum* Thom, is stated to yield anthracene on zinc dust distillation.⁴⁷

In the *Aspergillus glaucus* group physcion (4 : 5-dihydroxy-7-methoxy-2-methylantraquinone), first isolated from *A. glaucus* Link,⁴⁸ has now been found in sixteen other species or strains.⁴⁹ Physcion is of widespread occurrence in lichens and its isolation from moulds lends colour to the view that it and other lichen acids may owe their origin to the fungal half of the fungus-alga symbiont. Accompanying physcion in a number of *A. glaucus* species are related anthranols and erythroglaucin, $C_{16}H_{12}O_6$.⁴⁹ Erythroglaucin contains one methoxyl group and its trimethyl ether is identical with catenarin tetramethyl ether. From this fact and the insolubility of erythroglaucin in sodium carbonate solution and aqueous ammonia, reagents which readily dissolve catenarin, erythroglaucin is concluded to be 1 : 4 : 5-trihydroxy-7-methoxy-2-methylantraquinone.⁴²

Lichens.—As has been mentioned above, physcion is of frequent occurrence. It is found, for example, in the wall lichen *Xanthoria parietina*, where it is accompanied by chrysophanol. The Japanese lichen *Nephromopsis endocrocea* Asahina contains a red acid, which has been examined by Y. Asahina and F. Fuzikawa⁵⁰ and shown to be 4 : 5 : 7-trihydroxy-2-methylantraquinone-3-carboxylic acid. Solorinic acid, $C_{21}H_{22}O_6$, the orange colouring matter from the Alpine lichen *Solorina crocea*, is now formulated as 1 : 3 : 8-trihydroxy-6-methoxy-2-*n*-hexoylantraquinone. The main evidence for this structure is (1) the behaviour of the pigment on heating with hydriodic acid, *n*-hexoic acid and a substance, $C_{14}H_{10}O_5$, readily oxidised to 1 : 3 : 6 : 8-tetrahydroxyanthraquinone, being formed, (2) the presence of a ketonic carbonyl group, and (3) the production of 2-methylantracene on zinc dust distillation.⁵¹

Rhodocladonic acid, obtained from numerous *Cladonia* species, has been the subject of renewed investigation. According to present evidence it is to be regarded as the methyl ester of a tetrahydroxy-hydroxymethylantraquinonecarboxylic acid.⁵²

Insects.—The natural dyes cochineal, kermes, and lac-dye consist, or should consist, of the dried bodies of three species of insects (*Coccidæ*), and the pigments isolated from them have been the subject of extensive investigations in the past, but little new work on them appears to have been published in recent years. Kermesic acid, obtained from kermes (*Lecanium*

⁴⁵ T. Posternak, *Helv. Chim. Acta*, 1940, **23**, 1046.

⁴⁶ H. G. Hind, *Biochem. J.*, 1940, **34**, 67, 577.

⁴⁷ H. Igarasi, *J. Agric. Chem. Soc. Japan*, 1939, **15**, 225.

⁴⁸ H. Raistrick, R. Robinson, and A. R. Todd, *J.*, 1937, 80.

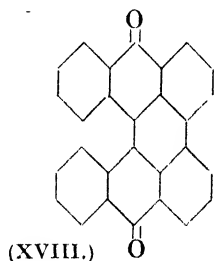
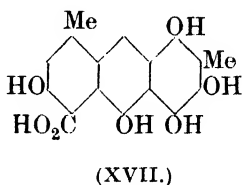
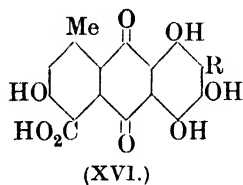
⁴⁹ J. N. Ashley, H. Raistrick, and T. Richards, *Biochem. J.*, 1939, **33**, 1291.

⁵⁰ *Ber.*, 1935, **68**, 1558.

⁵¹ G. Koller and H. Russ, *Monatsh.*, 1937, **69**, 54.

⁵² G. Koller and H. Hamburg, *ibid.*, 1936, **68**, 1558.

ilicis), was shown by degradative methods to have structure (XVI; R = COMe) as long ago as 1915,⁵³ and the work of O. Dimroth and his collaborators has largely clarified the structure of carminic acid, the colouring matter of cochineal (*Coccus cacti*). The results of degradative work on carminic acid are admirably described in a paper by O. Dimroth and H. Kämmerer,⁵⁴ where it is assigned the constitution (XVI; R = C₆H₁₁O₅), now generally accepted, in which the nature of the side chain C₆H₁₁O₅ is unknown beyond the fact that it contains four hydroxyl groups which can be acetylated, and that it confers optical activity on the molecule. It has been suggested that this grouping is -CO[CH·OH]₄-CH₃,⁵⁵ but the evidence for this view does not appear conclusive and such a structure is difficult to reconcile with the formation of coccinins (XVII) when carminic acid is fused with alkali.



Laccaic acid, C₂₀H₁₄O₁₀, the pigment of lac-dye (*Coccus laccae* = *Tachardia lacca*), has not been so extensively investigated as kermesic and carminic acids, but, like them, it is a complex anthraquinone derivative giving 1-methylantracene on zinc dust distillation.⁵⁶

Although not strictly speaking anthraquinones, the interesting compounds penicillipsin and hypericin are sufficiently closely related to be discussed here. Penicillipsin, C₃₀H₂₄O₈, the orange colouring matter of the mould *Penicillipsis clavariaeformis* Solms-Laubach,⁵⁷ is closely related to the polyhydroxyanthraquinones, since it yields emodin-anthranol when heated in air and 2-methylantracene on distillation with zinc dust. Solutions of the pigment in organic solvents containing small amounts of organic bases oxidise in presence of air and light, giving oxyphenicillipsin, C₃₀H₂₀O₉, a purple substance which is converted by visible light independent of the presence of air into an isomer crystallising in brown needles and showing a fiery red fluorescence in solution. It is tentatively suggested that penicillipsin may be a dimeride of emodin-anthranol, *i.e.*, a hexahydroxy-dimethyl derivative of a reduced *meso*-dianthrone, and that oxyphenicillipsin and its irradiation product are derivatives of helianthrone (XVIII), which they resemble in their properties.⁵⁷

Hypericin, the photodynamic colouring matter of St. John's wort (*Hypericum perforatum*) causing photosensitisation of animals eating that

⁵³ *Ann. Reports*, 1916, **13**, 113.

⁵⁴ *Ber.*, 1920, **53**, 471.

⁵⁵ I. Miyagawa, *A.*, 1927, 134.

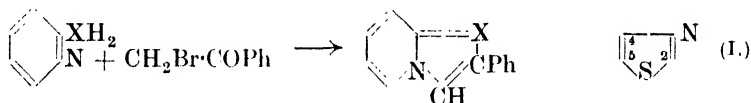
⁵⁶ A. Tschirch and F. Lüdy, *Helv. Chim. Acta*, 1923, **6**, 994.

⁵⁷ A. E. Oxford and H. Raistrick, *Biochem. J.*, 1940, **34**, 790.

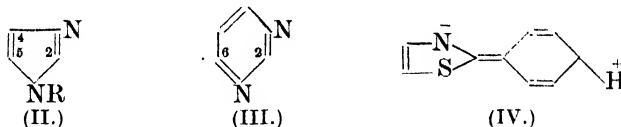
plant, has been investigated recently by two groups of workers.^{58, 59} In the most recent publication it is reported that hypericin can be separated into several distinct fractions by chromatography and that two of these seem to have the formulæ $C_{29}H_{22}O_8$ and $C_{31}H_{28}O_9$; the resemblances between hypericin and the *Penicillioptis* products is discussed and it is suggested that hypericin components are partially reduced polyhydroxyhelianthrones⁵⁹ and not mesodianthrones as was previously suggested.⁵⁸ A. R. T.

8. HETEROCYCLIC COMPOUNDS.

E. Ochiai¹ seeks to systematise the behaviour of heterocyclic rings of aromatic character : (a) A nitrogen atom linked $-N^-$, as in pyridine, leads to resonance with dipolar structures containing \bar{N}^- and hence to reactivity of appropriate nuclear positions towards anionoid substituting agents ($NaNH_2$), condensation of methyl side-chains with benzaldehyde, and ring closures with bromoacetophenone ($X = CH, N$) :



(b) The singly linked hetero-atom of furan, thiophen, and pyrrole, in resonance with structures containing, *e.g.*, $-\bar{O}^-$, entails more facile substitution by H_2SO_4 , HNO_3 , Br_2 , ArN_2X . These substitutions are facilitated even in pyridine by nuclear amino- or hydroxyl groups.



In thiazole (I) position 2 responds to the *a* group of reactions; the *b* group take place most reluctantly, but with hydroxyl or amino-substitution in 2, position 5 and less easily 4 may be attacked. The corresponding 1-position in benzthiazole behaves like 2 in thiazole. Reactions of the former type are difficult with 1-substituted glyoxalines (II), but the 4- and 5-positions are moderately susceptible to the latter. Pyrimidines (III) undergo the *a* reactions readily in positions 4, 6, and especially 2; and 2 : 5-dimethylpyrazine is aminated by sodamide.² *C*-Phenyl groups attached to thiazole or glyoxaline nuclei are nitrated in the *p*-position, structures such as (IV) having no decisive influence. The Friedel-Crafts reaction was successfully applied to 2-hydroxy-4-methylpyrazole and to 2-methylindolizine, but

⁵⁸ H. Brockmann, M. N. Haschad, K. Maier, and F. Pohl, *Naturwiss.*, 1939, **32**, 550.

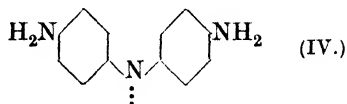
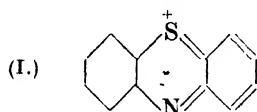
⁵⁹ N. Pace and G. Mackinney, *J. Amer. Chem. Soc.*, 1941, **63**, 2570.

¹ *Ber.*, 1939, **72**, 1470; *J. Pharm. Soc. Japan*, 1939, **59**, 20, 43, 97, 228, 256; 1940, **60**, 43, 55, 104; F. Nagasawa, *ibid.*, p. 219.

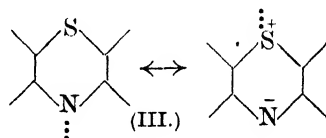
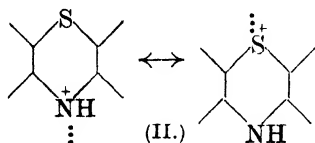
² R. R. Joiner and P. E. Spoerri, *J. Amer. Chem. Soc.*, 1941, **63**, 1929.

alkyl-glyoxalines and -pyrazoles, hydroxy- and amino-pyridines, 1-methyl-2-pyridone, and hydroxy- and amino-pyrimidines failed to react.

Semiquinone Radicals.³—The interconversion of phenazines and dihydro-phenazines often proceeds by way of a coloured "semiquinonoid" free radical. That similar equilibria are set up between semiquinones and oxidised (I) and reduced forms of phenoxazines, phenothiazines, and phenoselenazines, is now shown by potentiometric oxidative titration and confirmed in some cases by magnetochemical estimation of the radical form; there is no evidence of dimerisation of the radical.

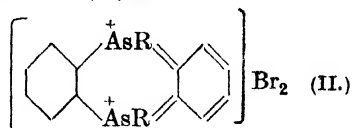
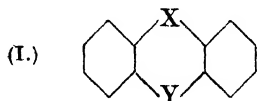


The greater stability of the radicals in slightly acid solution is attributed to the more favourable conditions for resonance in the system (II) as compared with (III). Contrast the minimal stability of the diphenylnitrogen radical, which lacks the co-operating sulphur atom.



In related dyes with amino- or hydroxyl groups in the 2- and 7-positions, the less basic ring nitrogen atom is neutralised, and the radicals reach their highest concentration, only in very acid media. Resonance is now possible with structures in which the odd electron is carried by the substituent, and the substances provide a connecting link with the radicals of the indamines (IV).

Stereochemistry.—The valency angles for 3-covalent arsenic being *ca.* 100°, the molecule (I; X = Y = As·C₆H₄Me) could exist in three configurations folded about the axis XY, two *cis* and one *trans* with respect to the tolyl groups, but for the exclusion of one form by the mutual interference of these groups. Two forms were in fact isolated; they gave the same tetrabromide, in which the ring system should now be planar (trigonal bipyramidal configuration for 5-covalent arsenic), and which on reduction yielded the one form to be expected for the salt-like dibromide (II).⁴

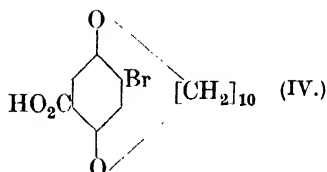
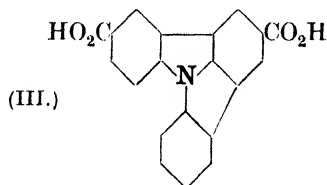


³ *Ann. Reports*, 1938, **35**, 322; L. Michaelis, S. Granick, and M. P. Schubert, *J. Amer. Chem. Soc.*, 1940, **62**, 204, 1802; 1941, **63**, 351; L. Michaelis and S. Granick, *ibid.*, p. 1636; L. Michaelis, *ibid.*, p. 2446.

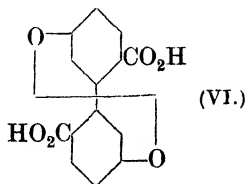
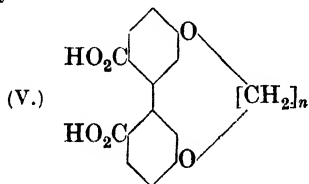
⁴ J. Chatt and F. G. Mann, *J.*, 1940, 1184.

Diphenylene dioxide and phenoxthionine (I; $X = O$, $Y = S$) have dipole moments, 0.64 and 1.09D., and presumably folded molecules⁵ (contrast *Ann. Reports*, 1935, 32, 131). According to preliminary reports⁶ on the crystallography and X-ray diffraction of several compounds of the type (I), a planar configuration is established for phenazine and admissible for diphenylene oxide.

The problem presented by such a structure as (III) has been considered from two standpoints. The tendency for the three central rings to be coplanar may impose a planar configuration on the nitrogen valencies;⁷ or else the consequent angle of $\gg 120^\circ$ between two of these valencies, with its resulting strain, may be decisive in favour of a non-planar arrangement with tetrahedral nitrogen bonds.⁸ Then the structure (III) would be asymmetric; it was synthesised, but its salts were unsuitable for resolution.



A new case of asymmetry is realised by the isolation of optically stable active forms of the acid (IV) in which the substituents prevent rotation of the benzene nucleus inside the large ring.⁹ In the related case (V) four possibilities are recognised:¹⁰ (1) For a very small value of n the molecule may be strained so that the carboxyl groups do not interfere. (2) With slightly larger n the unstrained molecule, having the carboxyls in the "cis" position but "staggered," should be resolvable, and also (3) when still larger n permits a "trans" configuration (VI) interconvertible with the *cis*-form, but no further rotation. (4) For large values (50–100) of n , the diphenyl system can rotate freely within the large ring. The compounds (V; $n = 8$ or 10)—case 3—have been resolved and show moderate optical stability.



⁵ K. Higasi, *Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1941, **38**, 331.

⁶ R. G. Wood and J. E. Crackston, *Phil. Mag.*, 1941, **31**, 62; R. G. Wood and G. Williams, *ibid.*, pp. 71 (with C. H. McCale), 115.

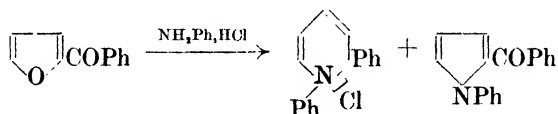
⁷ F. Lions and E. Ritchie, *J. Proc. Roy. Soc. N.S.W.*, 1939, **73**, 125; *J. Amer. Chem. Soc.*, 1939, **61**, 1927.

⁸ (Miss) H. G. Dunlop and S. H. Tucker, *J.*, 1939, 1945.

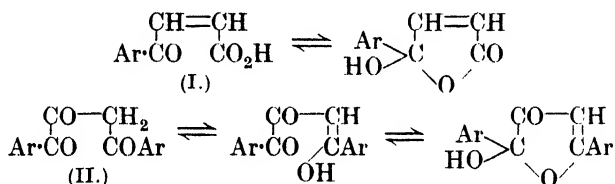
⁹ A. Lüttringhaus and H. Gralheer, *Naturwiss.*, 1940, **28**, 255.

¹⁰ R. Adams and N. Kornblum, *J. Amer. Chem. Soc.*, 1941, **63**, 188.

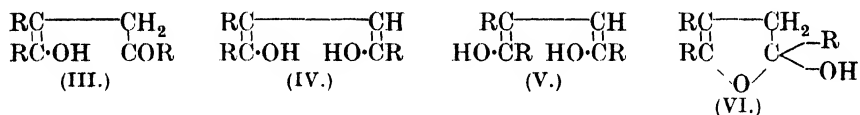
Ring-chain and Nuclear Transformations.—J. K. Juriev has studied the production of thiophenes and pyrroles from furan derivatives. Over a catalyst, best alumina at 400°, furan affords with ammonia pyrrole; with amines, *N*-substituted pyrroles; and with hydrogen sulphide, thiophen. Tetrahydrofuran gives analogous products also obtainable from tetramethylene glycol or its chlorohydrin. Pentamethylene oxide behaves similarly.¹¹ Many 2-furyl ketones react in the same way as furfural with the hydrochlorides of aromatic amines, giving arylpyridinium salts often accompanied by pyrrole derivatives :¹²



R. E. Lutz, following extensive studies of ring-chain tautomerism in β -aroylacrylic acids (I)¹³ and 1:2:4-triketones (II),¹⁴ suggests that the synthesis of furans from 1:4-diketones proceeds *via* the *mono-enol*.



The retarded keto-enolic transformations of mesityldimesitoylethane permitted the isolation of (III; R = C₆H₂Me₃) and the three other possible structurally and stereoisomeric mono-enols, and the di-enols (IV) and (V), as MgBr enolates and in some cases as free enols.



Of these, only (III) yielded the furan under mild conditions, presumably by dehydration of its lactol (VI).¹⁵

B. Oddo discusses the mechanism of the formation of pyridines from pyrroles by ring-enlargement;¹⁶ and T. Ajello considers that his¹⁷ con-

¹¹ *Ber.*, 1936, **69**, 440, 1002, 1944, 2492; *J. Gen. Chem. Russia*, 1937, **7**, 485, 1868, 2945; 1938, **8**, 116, 1934; 1939, **9**, 153, 590, 628, 1710; 1940, **10**, 31.

¹² W. Borsche, H. Leditschke, and K. Lange, *Ber.*, 1938, **71**, 957.

¹³ R. E. Lutz and M. Couper, *J. Org. Chem.*, 1941, **6**, 77.

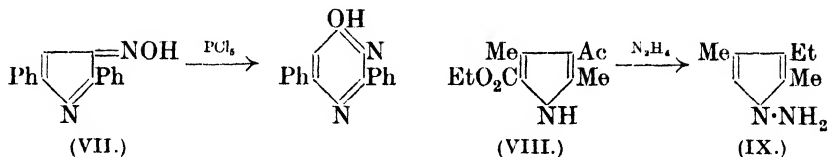
¹⁴ R. E. Lutz, J. M. Smith, and A. H. Stuart, *J. Amer. Chem. Soc.*, 1941, **63**, 1143.

¹⁵ R. E. Lutz and W. G. Reveley, *J. Amer. Chem. Soc.*, 1939, **61**, 1854; R. E. Lutz and C. J. Kibler, *ibid.*, 1940, **62**, 360.

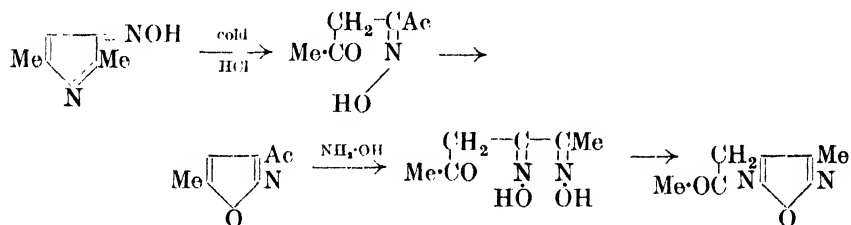
¹⁶ *Gazzetta*, 1939, **69**, 10.

¹⁷ *Ibid.*, p. 480; 1940, **70**, 504.

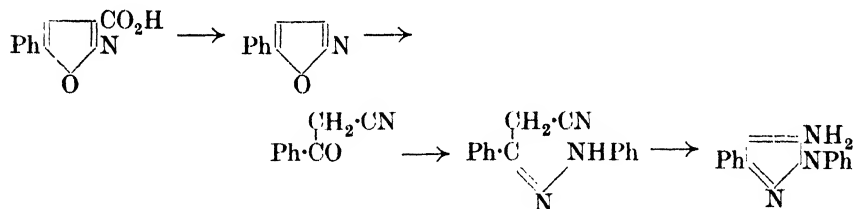
version of a pyrrole (VII) into a pyrimidine derivative is not a Beckmann change :



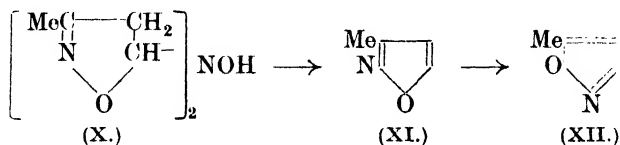
Numerous transformations result from ring-opening, followed by resynthesis. Attempted Kishner-Wolff reduction of (VIII) afforded (IX);¹⁸ and oximino-pyrrolenines may suffer the following series of changes :¹⁹



With phenylhydrazine, isooxazole-3-carboxylic acids can yield the corresponding *N*-phenylpyrazole-3-carboxylic acids, and also aminopyrazoles :²⁰



The "sesquioxime" of formylacetone, now formulated as (X),²¹ gives with alkali the isooxazoles (XI) and (XII), the former yielding the latter by hydrolysis and re-synthesis.



¹⁸ H. Fischer, H. Guggemos, and A. Schäfer, *Annalen*, 1939, **540**, 30.

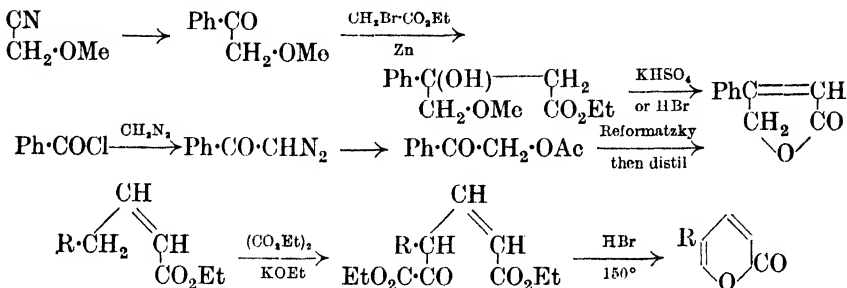
¹⁹ T. Ajello and S. Cusmano, *Gazzetta*, 1939, **69**, 207, 391.

²⁰ S. Cusmano, *ibid.*, pp. 594, 621; 1940, **70**, 86, 227, 235, 240.

²¹ R. Justoni, *ibid.*, pp. 796, 804.

Oxygen Ring Compounds.

Dioxadiene (I), prepared by treating tetrachlorodioxan with magnesium and magnesium iodide in butyl ether, is a highly unsaturated liquid, b. p. 75°, which is insoluble in water and polymerises when kept. Alkyldioxans are obtained from halogenodioxans and the Grignard reagent.²² As model experiments towards the synthesis of the aglycones of digitalis-strophanthus²³ and squills respectively, effective methods have been devised for the preparation of β -substituted Δ^a -butenolides²⁴ and 5-substituted α -pyrones :²⁵



On treatment with sodium carbonate, diazotised *o*-amino- β -phenylethyl alcohol affords 50% of coumaran (dihydrocoumarone); dihydrothionaphthen is obtained in excellent yield from the same diazo-compound, and dihydro-indole from the parent base.²⁶

Ozone attacks coumarones (or thionaphthens) normally, giving salicylic acid and aldehyde, with some catechol.²⁷ The hydrogenation of coumarin over Raney nickel affords in addition to octahydrocoumarin hexahydro-chroman, probably by way of *o*-hydroxy- γ -phenylpropyl alcohol, which is the main product of hydrogenation over copper chromite.²⁸

Vitamin E.²⁹—Interest in the tocopherols has led to renewed study of syntheses of the chroman and coumaran rings. In the condensation of phenols, especially quinols, with allyl alcohols or halides, or with dienes, it appears³⁰

²² R. K. Summerbell and R. R. Umhoefer, *J. Amer. Chem. Soc.*, 1939, **61**, 3016, 3020.

²³ W. D. Paist, E. R. Blout, F. C. Uhle, and R. C. Elderfield, *J. Org. Chem.*, 1941, **6**, 273.

²⁴ M. Rubin, W. D. Paist, and R. C. Elderfield, *ibid.*, p. 260; R. G. Linville and R. C. Elderfield, *ibid.*, p. 270.

²⁵ J. Fried and R. C. Elderfield, *ibid.*, pp. 566, 577.

²⁶ G. M. Bennett and M. M. Hafez, *J.*, 1941, 287.

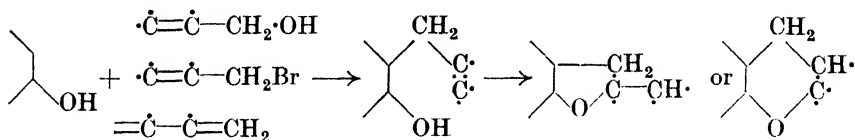
²⁷ A. von Wacek, H. O. Eppinger, and A. von Bézard, *Ber.*, 1940, **73**, 521.

²⁸ P. L. de Benneville and R. Connor, *J. Amer. Chem. Soc.*, 1940, **62**, 283, 3067.

²⁹ *Ann. Reports*, 1938, **35**, 309; L. I. Smith, *Chem. Reviews*, 1940, **27**, 287.

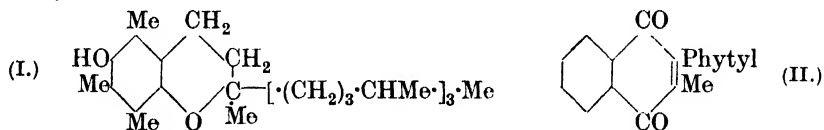
³⁰ L. I. Smith, H. E. Ungnade, H. H. Hoehn, and S. Wawzonek, *J. Org. Chem.*, 1939, **4**, 305, 311; L. I. Smith, H. E. Ungnade, J. R. Stevens, and C. C. Christman, *J. Amer. Chem. Soc.*, 1939, **61**, 2615; but see L. I. Smith and J. A. King, *ibid.*, 1941, **63**, 1887.

that the first stage is the *o*-allylphenol, produced without rearrangement in the allyl group:



The ring-closure of the allylphenol as an additive reaction of the double bond is directed in accordance with the Markovnikov rule so that, *e.g.*, the allyl compound gives the coumaran and the γ -dimethylallyl compound the chroman, and the monomethylallyl derivative gives a mixture.³¹ The free phenols are anti-oxidants, but *o*-allylphenyl acetate afforded chroman in presence of peroxides and methylcoumaran in their absence.³²

Methods have been worked out for the preparation in quantity of poly-alkylated quinones and quinols,³³ which have afforded numerous analogues of α -tocopherol (I) for biological tests.³⁴ α -Tocopherol made from synthetic phytol and possibly stereochemically distinct from (I) had the full activity of the vitamin.³⁵ The homologues with only two nuclear methyl groups,³⁵ of which the 5 : 8-isomeride is identical with natural β -tocopherol and the 7 : 8- with γ -,³⁶ were a little less potent than α -tocopherol, but a monomethylated compound was inactive. So also were the analogues of (I) with one or two isoprene units fewer in the side chain, but that with one unit more was quite active.³⁷ 2-Methyl- α -naphthaquinol and phytol³⁸ gave mainly products related to vitamin K₁ (II), but this with acid reducing agents afforded the naphthatocopherol, which showed moderate vitamin *E* as well as *K* activity.³⁹



³¹ P. Karrer, R. Escher, and H. Rentschler, *Helv. Chim. Acta*, 1939, **22**, 1287.

³² C. D. Hurd and W. A. Hoffman, *J. Org. Chem.*, 1940, **5**, 212.

³³ L. I. Smith, J. W. Opie, S. Wawzonek, and W. W. Prichard, *ibid.*, 1939, **4**, 318; O. H. Emerson and L. I. Smith, *J. Amer. Chem. Soc.*, 1940, **62**, 141; P. Karrer and O. Hoffmann, *Helv. Chim. Acta*, 1939, **22**, 654.

³⁴ Summary: H. M. Evans *et al.*, *J. Org. Chem.*, 1939, **4**, 376.

³⁵ P. Karrer and H. Fritzsche, *Helv. Chim. Acta*, 1939, **22**, 260; P. Karrer and B. H. Ringier, *ibid.*, p. 610; P. Karrer, H. Koenig, B. H. Ringier, and H. Salomon, *ibid.*, p. 1139; (Miss) A. Jacob, (Miss) M. Steiger, A. R. Todd, and T. S. Work, *J.*, 1939, 542.

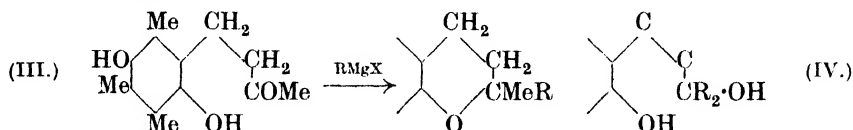
³⁶ O. H. Emerson and L. I. Smith, *J. Amer. Chem. Soc.*, 1940, **62**, 1869; P. Karrer and H. Rentschler, *Helv. Chim. Acta*, 1941, **24**, 304.

³⁷ P. Karrer and K. A. Jensen, *ibid.*, 1938, **21**, 1622; P. Karrer and K. S. Yap, *ibid.*, 1940, **23**, 581; 1941, **24**, 639.

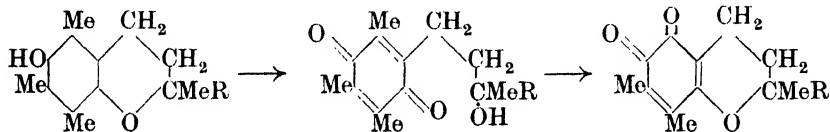
³⁸ (Miss) A. Jacob, F. K. Sutcliffe, and A. R. Todd, *J.*, 1940, 327.

³⁹ M. Tishler, L. F. Fieser, and N. L. Wendler, *J. Amer. Chem. Soc.*, 1940, **62**, 1982; M. Tishler and H. M. Evans, *J. Biol. Chem.*, 1941, **139**, 241.

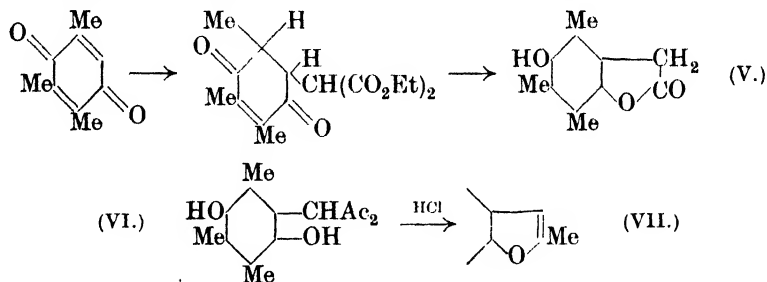
Hydroxy-coumarans and -pyrans are prepared from monohydric phenols in four steps, the sequence of which may be varied: diazo-coupling, followed by reduction to aminophenol; oxidation to quinone and reduction to quinol; allylation; ring closure.⁴⁰ W. John⁴¹ has developed methods for the synthesis, from simple quinols or otherwise, of ketones such as (III), which by Grignard reaction and dehydration afford chromans. The production of chromans from dihydrocoumarins or of chromens from coumarins by the Grignard reagent, in each case *via* the carbinol (IV), has been studied by several workers.⁴²



The tocopherols are oxidised by nitric acid to red compounds, used in their colometric determination, and now shown to be *o*-quinones:⁴³



L. I. Smith and co-workers have systematically studied the interaction of quinones and metallic enolates.⁴⁴ When one nuclear position is free, Michael addition of ethyl sodiomalonate takes place, and tautomeric change, followed by ring closure, affords (V). Acetylacetone gives (VI) and thence (VII), and ethyl acetoacetate a mixture of (V) and (VII).



⁴⁰ L. I. Smith, H. H. Hoehn, and A. G. Whitney, *J. Amer. Chem. Soc.*, 1940, **62**, 1863.

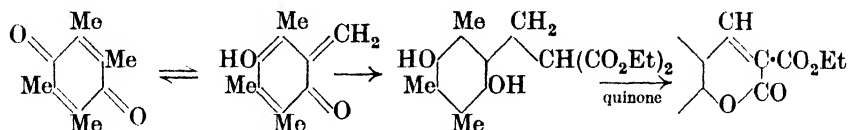
⁴¹ W. John and P. Günther, *Ber.*, 1939, **72**, 1649; 1941, **74**, 879, 890; W. John and M. Schmeil, *Ber.*, 1939, **72**, 1653.

⁴² W. John, P. Günther, and M. Schmeil, *Ber.*, 1938, **71**, 2637; L. I. Smith, H. E. Ungnade, and W. W. Prichard, *J. Org. Chem.*, 1939, **4**, 358; R. L. Shriner and A. G. Sharp, *ibid.*, p. 575; L. I. Smith and P. M. Ruoff, *J. Amer. Chem. Soc.*, 1940, **62**, 145.

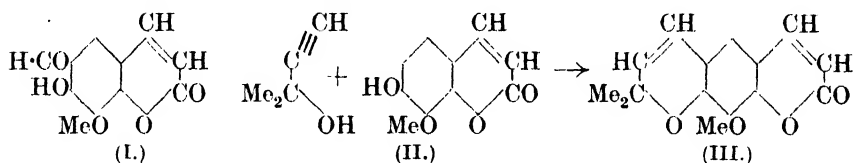
⁴³ L. I. Smith, (Miss) W. B. Irwin, and H. E. Ungnade, *J. Amer. Chem. Soc.*, 1939, **61**, 2424; L. I. Smith, P. M. Ruoff, and S. Wawzonek, *J. Org. Chem.*, 1941, **6**, 236.

⁴⁴ *J. Amer. Chem. Soc.*, 1938, **60**, 676; 1940, **62**, 133, 138; 1941, **63**, 612, 932. 937; *J. Org. Chem.*, 1939, **4**, 342; see also F. Bergel, (Miss) A. Jacob, A. R. Todd, and T. S. Work, *J.*, 1938, 1375, and *Ann. Reports*, 1937, **34**, 343.

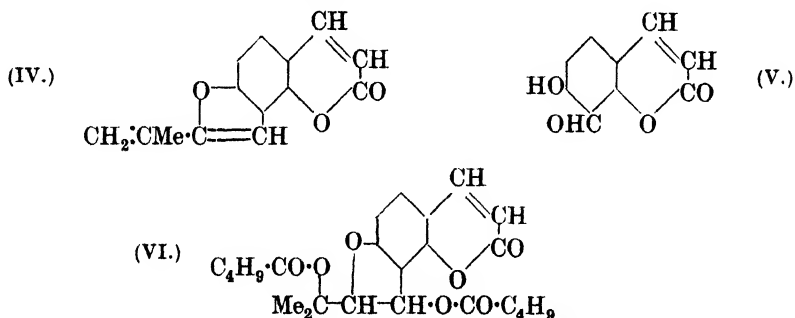
Tetrasubstituted quinones give coumarins with ethyl malonate, acetoacetate, or cyanoacetate, but diketones fail to react :



Natural Coumarins.—Luvangetin,⁴⁵ which occurs with other coumarins in *Luvunga scandens*, can be oxidised to α -hydroxyisobutyric acid and to the aldehyde (I). It is thus methoxyxanthyletin (III) and has been synthesised by heating methylbutinol with the product (II) of successive Hoesch and Perkin reactions on 2 : 6-dihydroxyanisole.



Athamantin,⁴⁶ from *Athamantum oreoselinum*, yields with acid oroselone (IV, not oroselone) and two molecules of *isovaleric* acid. By ozonisation, oroselone affords the aldehyde (V) and dihydro-oroselone gives *isobutyric* acid. Athamantin, which has an unreduced coumarin ring and yields acetone on oxidation after mild alkaline hydrolysis, is regarded as (VI). The hæmorrhagic agent in spoiled sweet clover has been isolated and identified as methylenebis-4-hydroxy-3-coumarinyl.⁴⁷



Nitrogen Ring Compounds.

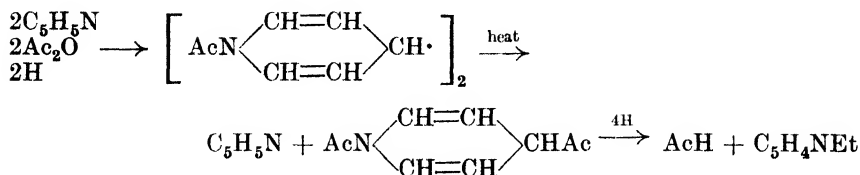
Pyridine Group.—The advantageous preparation of 4-ethylpyridine

⁴⁵ E. Späth, P. K. Bose, H. Schmid, E. Dobrovolsky, and A. Mookerjee, *Ber.*, 1940, **73**, 1361; E. Späth and H. Schmid, *Ber.*, 1941, **74**, 193.

⁴⁶ E. Späth, N. Platzer, and H. Schmid, *Ber.*, 1940, **73**, 709; E. Späth and H. Schmid, *ibid.*, p. 1309.

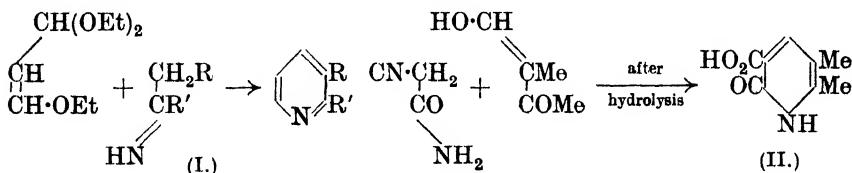
⁴⁷ M. A. Stahmann, C. F. Huebner, and K. P. Link, *J. Biol. Chem.*, 1941, **138**, 513.

from pyridine, acetic anhydride, and zinc dust proceeds⁴⁸ through the stages :



Numerous ketones condense with pyridine or quinoline in presence of magnesium or aluminium and mercuric chloride, giving tertiary α -pyridyl- or -quinolyl-carbinols.⁴⁹

The resemblance between the pyridine and thiazole rings suggested^{50, 51, 52} the preparation of pyridine derivatives related to vitamin B₁, some of which showed antineuritic activity, and led to the elaboration of general methods for the synthesis of 2 : 3-disubstituted pyridines. The relatively accessible ethoxycrotonaldehyde acetal condenses⁵⁰ with imines of the type (I), in which R is acyl or CN. Ethoxycrotonaldehyde behaves similarly, and 3-cyano-2-pyridones are obtained by using cyanoacetamide in place of (I). With ethyl malonate in place of the acetal, 4 : 6-dihydroxy-2 : 3-dialkylpyridines result, in which the hydroxyl groups can be replaced by chlorine and then by hydrogen.⁵¹ Alternatively, the substituents R and R' may be supplied in the molecule of a hydroxymethylene-ketone, and the ring synthesised in another sense (II).⁵¹ The corresponding synthesis from the more manageable ethoxalyl-ketones has also been effected.



An improved method for the pyrolysis of β -arylaminoacrotonic esters or the products of their alkylation has given numerous 2-methyl- and 3-alkyl-2-methyl-4-hydroxyquinolines.⁵³ The production of dihydroquinoline derivatives (III) from acid chlorides, hydrogen cyanide, and quinoline, and their

⁴⁸ J. P. Wibaut and J. F. Arens, *Rec. Trav. chim.*, 1941, **60**, 119.

⁴⁹ B. Emmert and E. Asendorf, *Ber.*, 1939, **72**, 1188; B. Emmert and E. Pirot, *Ber.*, 1941, **74**, 714.

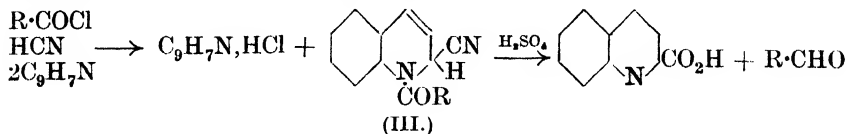
⁵⁰ A. Dornow *et al.*, *Ber.*, 1939, **72**, 563, 1548; 1940, **73**, 44, 78, 153, 156, 353.

⁵¹ J. Finkelstein and R. C. Elderfield, *J. Org. Chem.*, 1939, **4**, 365; (Miss) A. H. Tracy and R. C. Elderfield, *ibid.*, 1941, **6**, 54, 63, 70.

⁵² F. C. Schmelkes and R. R. Joiner, *J. Amer. Chem. Soc.*, 1939, **61**, 2562.

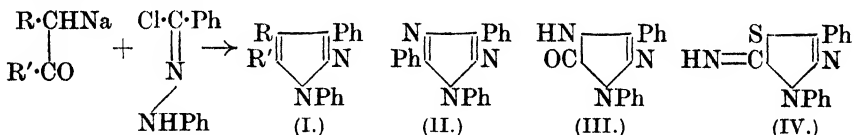
⁵³ G. K. Hughes and F. Lions, *J. Proc. Roy. Soc. N.S.W.*, 1938, **71**, 458; R. Gillis, F. Lions, and E. Ritchie, *ibid.*, 1940, **73**, 258.

hydrolysis to aldehydes, have been generalised as a preparative method for aliphatic and aromatic aldehydes from acids :⁵⁴

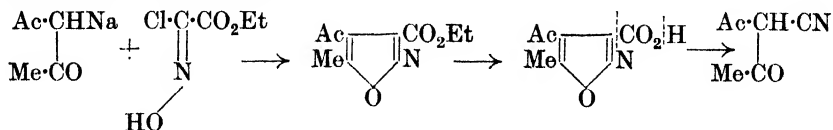


J. R. Bailey and his co-workers have examined the nitrogen bases of petroleum distillates.⁵⁵ The hydrochlorides of a "hydroaromatic" group, not yet effectively investigated, can be extracted from water by chloroform, leaving a series of quinoline homologues resolved by distillation, fractional or counter-current extraction by acid, fractional decomposition of sulphites, or crystallisation of salts. Quinoline and quinaldine, found with pyridine homologues in cracked gasoline, were absent from the straight-run distillates. These have afforded all the possible quinolines with methyl in the 2-, methyl or hydrogen in the 3- and 4-, and hydrogen, methyl, ethyl, or *n*-propyl in the 8-positions, except the 2 : 3 : 4-trimethyl and 2-methyl-8-propyl compounds. In addition, bases with *sec*.-propyl or *sec*.-butyl in position 8 have been isolated, several with ethyl in position 4, and two 7 : 8-benzoquinoline homologues. No 5-, 6-, or 7-alkylquinolines were encountered.

Azoles and Azines.—Pyrazole derivatives (I; R = CN, CO₂Et, Ac, Bz) are prepared from α -chlorobenzaldehydephenylhydrazone and the appropriate sodio-compounds; cyanoacetamide yields 4-cyano-5-amino-1 : 3-diphenylpyrazole. The same hydrazone gives with benzamidine the triazole (II), with potassium cyanate the triazolone (III), and with ammonium thiocyanate the compound (IV). α -Chlorobenzaldoxime affords in each case the analogous substance with O for NPh.⁵⁶



With the sodio-ketones, ethyl chloroisotonitrosoacetate gives esters which on hydrolysis lose carboxyl and then by a known ring-fission afford the cyano-derivative of the original ketone :

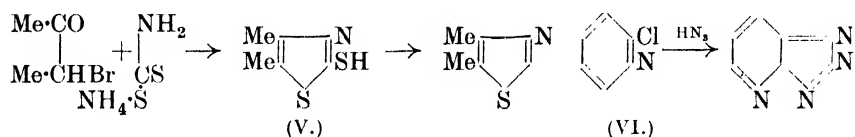


⁵⁴ J. M. Grosheintz and H. O. L. Fischer, *J. Amer. Chem. Soc.*, 1941, **63**, 2021.

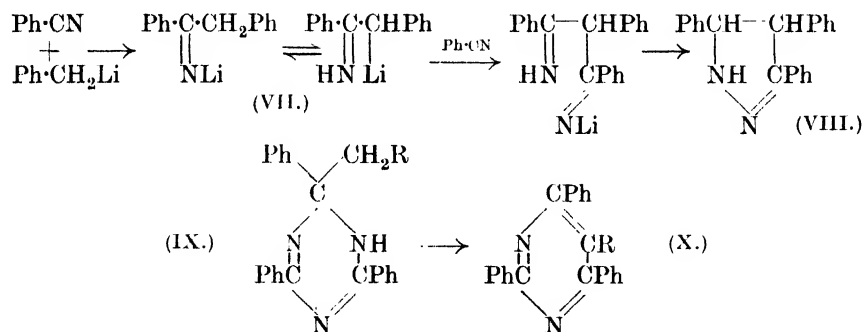
⁵⁵ *Ibid.*, 1930, **52**, 1239; 1931, **53**, 1002; 1933, **55**, 4136, 4141, 4143, 4145; 1934, **56**, 2741; 1937, **59**, 175; 1938, **60**, 763, 3025, 3028; 1939, **61**, 2609, 2612, 2613; 1940, **62**, 1967; 1941, **63**, 637, 639, 1364, 1365, 2331.

⁵⁶ R. Fusco, R. Justoni, C. Musante, and A. Quilico, *Gazzetta*, 1937, **67**, 3, 589; 1938, **68**, 59, 147, 331; 1939, **69**, 344, 353, 364, 523; L. Panizzi, *ibid.*, 1940, **70**, 89, 119.

C. H. Roeder and A. R. Day⁵⁷ conclude that the synthesis of benzimidazoles from acids and *o*-diamines proceeds *via* the monoacyl compound, the oxygen atom of which is eliminated with one hydrogen from each nitrogen. Dihydroglyoxalines and tetrahydropyrimidines have been prepared by distilling with lime the monoacyl derivatives obtained by treating ethylene- or trimethylene-diamine with esters.⁵⁸ 2-Thiolthiazoles (V), readily accessible from α -halogeno-ketones and ammonium dithiocarbamate, lose the thiol group on oxidation with nitric acid or hydrogen peroxide.^{1, 59} J. von Braun and W. Rudolph⁶⁰ modify the synthesis of tetrazoles from iminochlorides by using free hydrazoic acid, and have extended the process to 2-chloropyridine (VI). By a related method, "phenylcarbylamine chloride," $\text{Ph}\cdot\text{N}\cdot\text{CCl}_2$, and sodium azide yield 1-phenyl-5-azidotetrazole.⁶¹



Benzonitrile reacts with benzyl-lithium (and analogously with benzhydrysodium), giving a dihydroglyoxaline derivative (VIII). According to the mechanism suggested, the phenyl group of the original benzyl radical is necessary to confer acidity on the methylene hydrogen atoms of (VII). When phenyl- or alkyl-lithium is used, the primary product unites with two more molecules of nitrile, yielding a dihydrotriazine which gives on hydrolysis a phenyl ketone. The triazine (IX) from a primary alkyl-lithium can undergo a curious pyrolytic transformation to the pyrimidine (X) with loss of ammonia.⁶²



⁵⁷ *J. Org. Chem.*, 1941, **6**, 25.

⁵⁸ S. R. Aspinall, *J. Amer. Chem. Soc.*, 1939, **61**, 822 (with A. J. Hill), 3194; 1940, **62**, 2160.

⁵⁹ E. R. Buchman, A. O. Reims, and H. Sargent, *J. Org. Chem.*, 1941, **6**, 764.

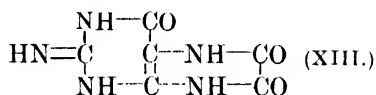
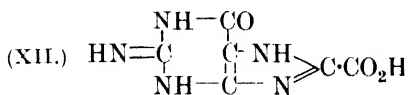
⁶⁰ *Ber.*, 1941, **74**, 264.

⁶¹ P. S. Pelkis and C. S. Dunaevskaja, *Mem. Inst. Chem. Ukrain. Acad. Sci.*, 1940, **6**, 163.

⁶² R. M. Anker and A. H. Cook, *J.*, 1941, 323.

L. Pauling and J. H. Sturdivant⁶³ suggested that cyameluric and hydromelonic acids, melam, melem, and melon, compounds derived directly or indirectly from pyrolysis of thiocyanogen derivatives, were related to a nucleus C_6N_7 in the same way as the cyanuric compounds to the C_3N_3 ring. For this nucleus they proposed the structure (XI) with the large calculated resonance energy of 150 Cals. C. E. Redemann and H. J. Lucas⁶⁴ show that hydromelonic acid, regarded as $C_6N_7(NH \cdot CN)_3$, like tricyanomelamine, $C_3N_3(NH \cdot CN)_3$, is too strong an acid for its dissociation constant to be measured, and cyameluric acid, $C_6N_7(OH)_3$, like cyanuric, is much weaker. Hydromelonic acid gives on hydrolysis cyameluric acid which has been converted into the chloride $C_6N_7Cl_3$ and into (mainly *N*-) alkyl derivatives and which yields one molecule only of cyanuric acid on further hydrolysis. Melam is now believed to be an imide $(NH_2)_2C_3N_3 \cdot NH \cdot C_3N_3(NH_2)_2$, and melem to be cyameluramide. Melon is probably a mixture of intermediate stages of "deammonation" between melem and a graphite-like $(C_3N_4)_n$.

Pterins.—These pigments of butterflies, wasps, and other insects, are not easily purified and characterised and are also difficult to combust. A careful revision of the analyses removes the necessity of assigning to them formulæ containing nineteen carbon atoms with three pyrimidine or purine nuclei.⁶⁵ Leucopterin is now formulated $C_6H_5O_3N_5$ (the trimethyl derivative gives the expected molecular weight in phenol)⁷⁰ and has been synthesised by fusing 2:4:5-triamino-6-hydroxypyrimidine with oxalic acid.⁶⁶ The formulæ (XII) and (XIII) are suggested for the substance.^{65, 68, 69} Condensation under milder conditions with dichloroacetic in place of oxalic acid gives xanthopterin $C_6H_3O_2N_5$,⁶⁹ which yields on oxidation leucopterin (not, as previously reported, an imino-leucopterin).⁶⁵ "Anhydroleucopterin" is shown to be a deoxyleucopterin, distinct from 6-deoxyleucopterin prepared from the 6-chloro-compound.⁶⁷ Guanopterin is identical with *isoguanine*.⁶⁶



T. S. S.

⁶³ *Proc. Nat. Acad. Sci.*, 1937, **23**, 615.⁶⁴ *J. Amer. Chem. Soc.*, 1939, **61**, 3420; 1940, **62**, 842.⁶⁵ H. Wieland and R. Purrmann, *Annalen*, 1940, **544**, 163.⁶⁶ R. Purrmann, *ibid.*, p. 182.⁶⁷ H. Wieland, A. Tartter, and R. Purrmann, *ibid.*, **545**, 209.⁶⁸ C. Schöpf, *Naturwiss.*, 1940, **28**, 478.⁶⁹ R. Purrmann, *Annalen*, 1940, **546**, 98.⁷⁰ H. Wieland and P. Decker, *ibid.*, 1941, **547**, 180.

BIOCHEMISTRY.

SOME of the most interesting developments in biochemistry during the past year have had to do with the following topics: vitamins, intermediate metabolism of proteins, biochemistry of muscle, intracellular gels, biochemical systems in plants, carboxylation and decarboxylation in bacterial systems, metabolism of moulds. The specialists invited to cover the corresponding reviews in these pages are Dr. L. J. Harris, Dr. A. Neuberger, Dr. Dorothy Needham, Dr. J. F. Danielli, Dr. F. W. Norris, Dr. H. Krebs and Dr. Marjory Stephenson, and Professor H. Raistrick.

1. VITAMINS.

In consequence perhaps of the special needs of war-time most attention seems to have been given of late to two problems of immediate practical importance, namely, the devising of methods, first for the more accurate determination of vitamins in foodstuffs (see also the Report on Analytical Chemistry), and secondly for assessing the nutritional status of humans. The old idea that vitamins were only "qualitative" factors, and that the amount present in the food did not matter provided they were there in the merest trace, has gone by the board. A definite minimal quantity of each vitamin is now recognised as needed to prevent deficiency disease, and a larger quantity to prevent "subclinical deficiencies." Dietetic essentials not recognised until a few years ago are now well established and have already found important clinical uses; such are nicotinamide, riboflavin and vitamin K: knowledge is accumulating too about the significance of the still "newer" vitamins, for example, adermin (vitamin B₆), biotin (vitamin H), choline, *p*-aminobenzoic acid, inositol. Particularly interesting is the recent work relating to choline, the absence of which produces remarkable changes in the animal organism.

Water-soluble Vitamins: Vitamin B₁.

Methods of Assay.—Probably the most comprehensive study of technique for estimating a vitamin in foodstuffs which has so far appeared is that of L. J. Harris and Y. L. Wang.¹ They describe a series of modifications in the thiochrome method, based on the procedure previously used for urine.² Their results were checked by biological assays, three different methods being used, on more than 50 foodstuffs of all types. With the improvements recommended, the chemical and biological values generally differed by less than 15%. The reliability of this modified chemical method has also been confirmed by E. C. Slater³ and other workers. Another procedure

¹ *Biochem. J.*, 1941, **35**, 1050; *Chem. and Ind.*, 1942, **61**, 27.

² Y. L. Wang and L. J. Harris, *Biochem. J.*, 1939, **33**, 1356; 1941, **35**, 1068.

³ *Aust. J. Exp. Biol. Med.*, 1941, **19**, 29.

which is being made increasingly specific, and is likewise relatively simple to perform, depends on a measurement of the carbon dioxide evolved during the fermentation of yeast, which is stimulated by the addition of vitamin B₁. To distinguish between specific fermentation due to the vitamin and the non-specific "blank," tests are done before and after addition of ferrieyanide, or better of sulphite, to the unknown. These substances destroy the vitamin and the products formed have no activity in the fermentation.⁴

Assessment of Level of Nutrition.—Several workers⁵ have confirmed the observation⁶ that an elevation in pyruvic acid may be used to record the presence of a deficiency of vitamin B₁ in the experimental animal. For detecting partial deficiencies in the human subject, as in animals, tests of tolerance to carbohydrate loading⁷ were recommended and these have proved of practical use clinically.⁸

Rôle of Vitamin B₁ in Carbohydrate Metabolism.—Observations of E. S. G. Barron and co-workers⁹ just published may help to remove confusion about the chemical reactions brought about in mammalian tissues by vitamin B₁. It has long been accepted that in yeast, vitamin B₁, in the form of its pyrophosphate ester, is the co-enzyme for the decarboxylation of pyruvic acid, an essential intermediate in the metabolism of carbohydrates. In animal tissues the reactions have been found much less simple to study. The point is made in the papers just mentioned that in order to examine the effect of vitamin B₁ on animal tissues *in vitro*, it is necessary to incubate the vitamin first with the tissue, in order presumably to convert it into the active pyrophosphate derivative. With this proviso, it can then be shown that vitamin B₁ catalyses a variety of reactions, such as oxidation, dismutation and condensation, all of which, however, seem to involve decarboxylation at some stage. In the latter respect, therefore, animal tissues now seem to come fundamentally into line with yeast. Much other important work¹⁰ on the biochemical function of vitamin B₁ as a co-enzyme has appeared, and it will be more convenient to review the whole problem when a longer perspective is possible after the lapse of another year.

⁴ A. S. Schultz, L. Atkin, and C. N. Frey, *J. Biol. Chem.*, 1940, **136**, 713; A. S. Schultz, L. Atkin, C. N. Frey, and R. R. Williams, *J. Amer. Chem. Soc.*, 1941, **63**, 633; H. Laser, *Biochem. J.*, 1941, **35**, 488.

⁵ M. E. Shills, H. G. Day, and E. V. McCollum, *J. Biol. Chem.*, 1941, **139**, 145; H. A. Harper and H. J. Deuel, *ibid.*, 1941, **137**, 233.

⁶ G. G. Banerji and L. J. Harris, *Biochem. J.*, 1939, **33**, 1346.

⁷ See *Ann. Reports*, 1940, **37**, 387.

⁸ E. O'S. Elsom, F. D. H. Lukems, and E. H. Montgomery, *J. Clin. Invest.*, 1940, **19**, 153.

⁹ E. S. G. Barron and C. M. Lyman, *J. Biol. Chem.*, 1941, **141**, 951; E. S. G. Barron, C. M. Lyman, M. A. Lipton, and J. M. Goldinger, *ibid.*, p. 957; E. S. G. Barron, J. M. Goldinger, M. A. Lipton, and C. M. Lyman, *ibid.*, p. 975.

¹⁰ *E.g.*, F. J. Stare, M. A. Lipton, and J. M. Goldinger, *ibid.*, p. 981; H. A. Sober, M. A. Lipton, and C. A. Elvehjem, *ibid.*, 1940, **134**, 605; M. A. Lipton and C. A. Elvehjem, *ibid.*, 1940, **136**, 637; S. Ochoa, *ibid.*, 1941, **138**, 751; J. H. Quastel and D. M. Webley, *Biochem. J.*, 1941, **35**, 192.

Vitamin B₂ Complex.

Riboflavin.—The polarograph is proving of increasing use in the determination of vitamins,¹¹ and offers a convenient method, for example, with riboflavin.¹² With attention to detail, the chemical method (measurement of fluorescence) also gives results in agreement with biological assays.¹³

Cheilosis (angular stomatitis) has in the past year or two come to be considered as the characteristic sign of riboflavin deficiency in man, but to judge from the clinical observations of T. E. Machella¹⁴ it may be a relatively non-specific lesion, the primary cause being sometimes a deficiency of vitamin B₆, sometimes nicotinic acid or sometimes even ascorbic acid.

Nicotinamide.—Pellagra has been very prevalent in Spain since the civil war,¹⁵ and, possibly as a result of the present war or perhaps only as a result of better searching for it, an increased incidence is recorded in Northern Ireland.¹⁶ To assess the level of nutrition in the anti-pellagra vitamin,¹⁷ the modified procedure recommended by E. Kodicek and Y. L. Wang¹⁸ involves dosing with nicotinamide while the patient is kept on a diet free from trigonelline, and measurement of the urinary response in excretion of trigonelline plus nicotinic acid.¹⁹ An observation which may throw light on the mode of action of the vitamin is that it inhibits the breakdown of co-enzyme by the nucleotidases present in animal tissues.²⁰

Microbiological Methods.—Relatively specific methods now exist for differentiating and determining the various components of the vitamin-B₂ complex by means of their stimulating action on various micro-organisms under appropriately standardised conditions. Recent literature describing such methods for pantothenic acid²¹ and for nicotinic acid²² may be cited as excellent examples from an important and quickly growing literature.

Vitamin C.

Methods of Assay.—Further evidence²³ is available of the applicability of the polarograph for estimating vitamin C.²⁴ A source of error which had too often been overlooked in the chemical determination of vitamin C

¹¹ E. Kodicek and K. Wenig, *Nature*, 1938, **142**, 35.

¹² J. J. Lingane and O. L. Davis, *J. Biol. Chem.*, 1941, **137**, 567.

¹³ F. O. Van Duyne, *ibid.*, 1941, **139**, 207.

¹⁴ *Amer. J. Med. Sci.*, 1942, **1**, 114.

¹⁵ Quoted by *Lancet*, 1941, ii, 458.

¹⁶ J. Deeny, *Brit. Med. J.*, 1942, i, 157.

¹⁷ Cf. L. J. Harris and W. D. Raymond, *Biochem. J.*, 1939, **33**, 2037.

¹⁸ *Nature*, 1941, **148**, 23.

¹⁹ See further W. A. Perlzweig, H. P. Sarett, and J. W. Huff, *J. Biol. Chem.*, 1941, **140**, proc. C; H. P. Sarett, *J. Nutrition*, 1942, **23**, 23.

²⁰ P. J. G. Mann and J. H. Quastel, *Nature*, 1941, **147**, 326; *Biochem. J.*, 1941, **35**, 502.

²¹ M. J. Pelczar and J. R. Porter, *J. Biol. Chem.*, 1941, **139**, 111.

²² H. Isbell, J. G. Wooley, R. E. Butler, and W. H. Sebrell, *ibid.*, p. 499; E. E. Snell and L. D. Wright, *ibid.*, p. 675.

²³ T. Østerud, *Tek. Ukeblad*, 1939, **86**, 216.

²⁴ Cf. E. Kodicek and K. Wenig, *Nature*, 1938, **142**, 35.

is that any sulphur dioxide present as a preservative in fruit pulps, juices, etc., will seriously interfere unless special precautions²⁵ are taken.

War-time Considerations.—With the diminished supply of imported fruits, our bodies' reserves of vitamin C are likely to be far lower than they were before the war, and it is therefore useful to have the authoritative memorandum dealing with the preparation and cooking of green vegetables, which gives rules for treatments calculated to cause the least loss.²⁶ In cooking sour fruits a limited amount of alkali (sodium bicarbonate) can safely be added to save sugar.²⁷ Valuable compilations by M. Olliver²⁸ and W. B. Adam²⁹ deal comprehensively with the effects of cooking and canning respectively on the nutritive value of vegetables.

"Partial Deficiency" of Vitamin C.—Various views are taken about the reality of sub-clinical deficiency. On the one hand S. S. Zilva³⁰ has argued: "As far as the civilian population of this country, leading a normal life, is concerned, the natural supply of vitamin C during the greater part of the year is so superabundant that, even allowing the widest margin for destruction in the cooking and the preparation of the food, the intake is more than adequate to supply the vitamin C requirements." On the other hand, tests in Germany proved that the addition of extra vitamin C (50 mg. per day) to the diet of over a million children increased their resistance to infection and improved their yearly gains in weight and height—although there had been little or no actual clinical survey.³¹ Similar tests have been done in a large training school in Britain on 1500 adolescents: in the control group receiving no added vitamin C there occurred 17 cases of pneumonia and 16 of rheumatic fever, whereas there was no case of either in the group given added vitamin C; tonsillitis occurred in both groups but the average duration of illness in the control group was much longer, the difference being of undoubted statistical significance.^{31a} Addition of vitamin C to the diet has also been found to diminish the incidence of gingivo-stomatitis, or aid in its cure,^{31b} and to promote healing after dental extraction.^{31c} Again the healing of wounds after surgical operation is usually found to be better in subjects receiving ample vitamin C³² than in those whose intake is lower. There is in fact ample evidence that in man, as in animals, sub-clinical deficiency of vitamins produces a variety of somewhat ill-defined but none the less real faults in nutrition³³—for vitamin C these may include sub-

²⁵ L. W. Mapson, *Chem. and Ind.*, 1941, **60**, 802.

²⁶ Accessory Food Factors Committee, Medical Research Council, *Brit. Med. J.*, 1941, ii, 26.

²⁷ L. W. Mapson and J. Barker, *Chem. and Ind.*, 1941, **60**, 661.

²⁸ *Ibid.*, p. 586.

²⁹ *Ibid.*, p. 627.

³⁰ *Biochem. J.*, 1941, **35**, 1240.

³¹ *Bull. War Med.*, 1941, **2**, 6.

^{31a} A. J. Glazebrook and S. Thomson, *J. Hyg.*, 1942, **42**, 1.

^{31b} F. S. Roff and A. J. Glazebrook, *J. Roy. Nav. Med. Serv.*, 1939, **25**, 340; *Brit. Dent. J.*, 1940, **68**, 135; H. G. Campbell and R. P. Cook, *Brit. Med. J.*, 1941, i, 360.

^{31c} H. G. Campbell and R. P. Cook, *Brit. Dent. J.*, 1942, **72**, 6.

³² C. C. Lund and J. H. Crandon, *Ann. Surgery*, 1941, **114**, 776.

³³ See L. J. Harris, *Proc. Nutrition Soc.*, 1941, No. 1; also *Food*, 1942, **11**, 23.

optimal growth, diminished resistance to infection, impaired formation of scar tissues, and irregularities in teeth and gums.

Therapeutic Uses of Vitamin C.—Apart from its value in securing the adequate healing of wounds,³² there is evidence also that an abundant supply of vitamin C prolongs the life of experimental animals submitted to severe bleeding³⁴ or to low oxygen tensions.³⁵ This it may do by securing a more adequate supply of oxygen to the tissues.

Mode of Action of Vitamin C.—In the last-mentioned connection it may be noted that S. S. Zilva and his colleagues³⁶ have confirmed the finding of D. C. Harrison³⁷ that addition of ascorbic acid *in vitro* to the liver tissues of scorbutic animals augments their uptake of oxygen. The exact meaning of this finding is not yet clear, but G. A. Snow and S. S. Zilva discuss its possible connection with carbohydrate metabolism. Various types of enzyme systems are however also activated by vitamin C, *e.g.*, liver esterase, succinic dehydrogenase, and to a less extent cytochrome oxidase, and phosphatases from the kidney and intestine;³⁸ the degree of specificity of such activations still remains in doubt. In cauliflower juice dehydroascorbic acid is reduced by SH-glutathione, and the enzyme which catalyses the reaction has now been separated: it is suggested that it may have a rôle as an "end system" in plants.³⁹

Fat-Soluble Vitamins: Vitamin A.

Factors influencing Utilisation of Vitamin A.—It is becoming apparent that the efficiency with which vitamin A or carotene prevents deficiency disease in animals (and presumably in humans) varies with other factors in the diet: *e.g.*, the utilisation of carotene by the rat depends on the chemical nature of the oil administered with it;⁴⁰ prolonged deficiency of vitamin E causes a secondary deficiency of vitamin A;⁴¹ and the quantity of food consumed of course also influences the growth rate with any given intake of vitamin A.⁴²

Assessment of Level of Nutrition.—S. Yudkin⁴³ has made a careful re-investigation of dark adaptation as a means of detecting sub-clinical deficiency of vitamin A. Of 24 subjects tested for "night blindness," all except three improved with vitamin A. The method, which is in any case relatively specific, can thus be made completely so by taking as the criterion an improvement or otherwise after dosing with vitamin A.⁴⁴ S. Yudkin⁴³

³⁴ C. P. Stewart, J. R. Learmonth, and G. A. Pollock, *Lancet*, 1941, i, 818.

³⁵ B. G. B. Lucas, quoted by J. M. Peterson, *Nature*, 1941, **148**, 84.

³⁶ A. E. Kellie and S. S. Zilva, *Biochem. J.*, 1941, **35**, 783; G. A. Snow and S. S. Zilva, *ibid.*, p. 878.

³⁷ *Ibid.*, 1933, **27**, 1501.

³⁸ C. J. Harrer and C. G. King, *J. Biol. Chem.*, 1941, **138**, 111.

³⁹ E. M. Crook, *Biochem. J.*, 1941, **35**, 226.

⁴⁰ W. C. Sherman, *J. Nutrition*, 1941, **22**, 153.

⁴¹ A. W. Davies and T. Moore, *Nature*, 1941, **147**, 794.

⁴² K. D. Muelder and E. Kelly, *J. Nutrition*, 1941, **21**, 13.

⁴³ *Lancet*, 1941, ii, 787.

⁴⁴ See, *e.g.*, *Ann. Reports*, 1939, **36**, 338.

emphasises that it may be necessary to give massive doses, and that with smaller doses especially the cure may be only transient. For any given subject there is a critical low level for the vitamin A in the blood, and below it dark adaptation is adversely affected; unfortunately, however, there appeared to be no such standard level applicable for all subjects. Benz-drine or alcohol produced transient improvement, but the supposed adjuvant action of vitamin C⁴⁵ could not be confirmed. An alternative procedure, biomicroscopy with the slit-lamp,⁴⁶ has been used by H. D. Kruse and his fellow investigators in the course of their impressive surveys on the evaluation of nutritional status;⁴⁷ but Kruse is rightly at pains to point out that the ocular lesion (keratosis) is not the sole, first or most important abnormality: "xerophthalmia is not synonymous with avitaminosis A."

Effects of Deficiency.—E. Mellanby⁴⁸ has published the detailed account of his observations on the skeletal changes produced in young dogs by deficiency of vitamin A. The bony overgrowths in the skull and vertebral column may produce deformities in the brain and spinal cord. Mellanby concludes that vitamin A controls the degree of activity of the osteoblasts and osteoclasts.

Vitamin A in Blood and Urine.—Reference to vitamin A in the blood and its connection with dark adaptation in humans has been made above. Similarly it has been shown that in dogs the level of vitamin A in the blood is proportional to the intake in the diet, and during depletion the level drops gradually: a low level in the blood cannot however be taken to indicate that the reserves have become depleted.⁴⁹ In humans vitamin A is not found in the urine except in certain diseases, notably pneumonia and chronic nephritis. It is probably significant that in these two diseases, among others, there is a great disappearance of the reserves of vitamin A from the liver. A strange phenomenon, still lacking explanation, is that in dogs, by contrast with humans, vitamin A is a normal constituent of the urine.⁵⁰

Vitamin D.

Influence on Metabolism.—Extended observations by S. H. Liu⁵¹ in China on patients with osteomalacia have proved once again that vitamin D is the primary factor controlling cure of the disease, and have confirmed also that its mode of action is to decrease the faecal loss of calcium.⁵²

Factors influencing Rachitogenesis.—It has been emphasised⁵³ that fat is one of many factors—others include the acid-base reaction, the Ca-P ratio, presence of heavy metals, sugars, etc.—which have an effect on the pro-

⁴⁵ Cf. C. P. Stewart, *Edinburgh Med. J.*, 1941, **48**, 217.

⁴⁶ *Milbank Memorial Fund Quarterly*, 1941, **19**, 207.

⁴⁷ *Ibid.*, 1939—1941. ⁴⁸ *J. Physiol.*, 1941, **99**, 467.

⁴⁹ P. C. Leong, *Biochem. J.*, 1941, **35**, 806.

⁵⁰ N. R. Lawrie, T. Moore, and K. R. Rajagopal, *ibid.*, p. 825.

⁵¹ *Chinese Med. J.*, 1940, **57**, 101.

⁵² Cf. L. J. Harris, *Lancet*, 1932, i, 1031.

⁵³ A. Knudson and R. J. Floody, *J. Nutrition*, 1940, **20**, 317.

duction or healing of rickets. Phytic acid is another such, and important, factor, and to it the rickets-producing action of cereals is attributable. The cause of the deleterious action of the phytic acid seems to be partly that it precipitates the calcium in the intestine and partly that it renders the calcium non-ionised and thus impedes its absorption.⁵⁴ But, fortunately, when wheat flour is baked with yeast, an enzyme, phytase, present in the flour largely destroys the phytic acid.⁵⁵

Other Fat-soluble Vitamins.

Vitamin E.—Standards and methods. Of importance to all research chemists and analysts working on vitamins is the adoption of racemic α -tocopherol acetate as the international standard for vitamin E.⁵⁶ The two chemical methods for estimating the vitamin, potentiometrically with auric chloride, or colorimetrically with the ferric reagent, have been systematically reinvestigated by Karrer and his colleagues and found to give results in satisfactory agreement.⁵⁷

Symptoms of avitaminosis E. It is pleasing for once to be able to record a diminution instead of an increase in the apparent number of the vitamins. A variety of symptoms in various species, sometimes attributed in the past to lack of still unidentified factors, have been found to respond to synthetic vitamin E. There is accordingly no longer any need to call in hypothetical new vitamins to account for the following disorders: "nutritional encephalomalacia" of chicks, "nutritional myopathy" of ducklings and "gizzard disease" of turkeys, "muscular dystrophy" of guinea pigs, rabbits and young rats,⁵⁸ generalised oedema in chicks,⁵⁹ "alimentary exudative diathesis" in chicks.⁶⁰

Clinical uses. Although admittedly lack of vitamin E causes muscular atrophy in experimental animals, it seems dangerous to jump to the conclusion, as has sometimes been done, that vitamin E is therefore useful in a wide range of neuromuscular disorders in man. Controversy on this issue still continues.⁶¹ For habitual abortion in women, however, a statistical treatment of the results of treatment is distinctly encouraging.⁶²

Vitamin F.—Physiological action. An observation which for the first time promises to throw light on the mode of action of vitamin F (nutri-

⁵⁴ E. F. Yang, *Nature*, 1940, **145**, 745; D. C. Harrison and E. Mellanby, *ibid.*, p. 745.

⁵⁵ E. M. Widdowson, *ibid.*, 1941, **148**, 219.

⁵⁶ E. M. Hume, *ibid.*, pp. 472, 473.

⁵⁷ P. Karrer, W. Jaeger, and H. Keller, *Helv. Chim. Acta*, 1940, **23**, 464; see also A. Emmerie, *Rev. Trav. chim.*, 1940, **59**, 246; F. Grandel and H. Newman, *Z. Unters. Lebensm.*, 1940, **79**, 57.

⁵⁸ A. M. Pappenheimer, *J. Mt Sinai Hosp., N.Y.*, 1940, **7**, 65; H. M. Evans and G. A. Emerson, *Proc. Soc. Exp. Biol., Med.*, 1940, **44**, 636; C. G. Mackenzie, J. B. Mackenzie, and E. V. McCollum, *J. Nutrition*, 1941, **21**, 225.

⁵⁹ H. R. Bird and T. G. Culton, *Proc. Soc. Exp. Biol. Med.*, 1940, **44**, 543.

⁶⁰ H. Dam and J. Glavind, *Naturwiss.*, 1940, **28**, 207.

⁶¹ See, e.g., *Lancet*, 1941, ii, 619; *Brit. Med. J.*, 1941, ii, 618.

⁶² A. L. Bacharach, *Brit. Med. J.*, 1940, i, 890; 1941, ii, 709.

tionally essential fatty acids) is that in its deficiency there is an impaired absorption of ordinary fats.⁶³

Vitamin K.—*Clinical uses.* Reports continue to appear stressing the value of vitamin K in preventing hæmorrhage after operation for obstructive jaundice, or in new-born infants; the comprehensive monograph on this vitamin by H. R. Butt and C. T. Snell⁶⁴ will be welcomed.

The Newer Vitamins.

Enumeration.—The “vitamin-B₂ complex” includes, by definition, riboflavin and nicotinamide (pellagra-preventing factor), both of which have already been referred to above, and also adermin (pyridoxin, vitamin B₆) and pantothenic acid (filtrate factor, bios IIA), which have been discussed in a recent issue of these Reports.⁶⁵ Other vitamins more recently characterised, which could logically be classified as of the “B₂ group,” include vitamin H (biotin, bios IIB, co-enzyme R), choline, inositol (bios I), and *p*-aminobenzoic acid (possibly identical with the “anti-grey-hair factor”).

Vitamin H (Biotin, Bios IIB).—Vitamin H is the factor needed by rats or chicks for protection against the nutritional injury which arises when their diet contains much raw egg-white. It is identical with biotin (or bios IIB, a factor needed by yeast and other micro-organisms) and also with the so-called “co-enzyme R” which stimulates the growth of micro-organisms in the nodules of the roots of certain leguminous plants.⁶⁶ The action of the raw egg-white in inducing the deficiency in rats has been traced to a component in the crude protein which unites with the vitamin H and thus renders it unavailable to the organism.⁶⁷ This component has been named “avidin,” and methods have been worked out for fractionating it, and estimating it.⁶⁸ Vitamin H itself has also been isolated and its empirical formula established (C₁₁H₁₈O₃N₂S);⁶⁹ its behaviour to various reagents has been studied,⁷⁰ and it has been shown to be a carboxylic acid

containing an *NN'*-substituted cyclic urea group and a thioether linkage (annexed formula).⁷¹ As to the physiological nature of the “egg-white injury” and the action of vitamin H in preventing it, it may perhaps be of significance that G. Gavin and E. W. McHenry⁷² have found that biotin given to rats induces fatty livers, whereas the simultaneous administration of egg-white (or of inositol) prevents this effect.

Choline.—Perhaps the most spectacular work on vitamins during the past two or three years is that relating to choline. This substance is under

⁶³ R. H. Barnes, E. S. Miller, and G. O. Burr, *J. Biol. Chem.*, 1941, **140**, 773.

⁶⁴ “Vitamin K,” 1941.

⁶⁵ *Ann. Reports*, 1940, **37**, 389, 390.

⁶⁶ *Ibid.*, p. 302.

⁶⁷ R. E. Eakin, E. E. Snell, and R. J. Williams, *J. Biol. Chem.*, 1940, **136**, 801.

⁶⁸ *Idem, ibid.*, 1941, **140**, 535.

⁶⁹ V. du Vigneaud, K. Hofmann, D. B. Melville, and P. György, *ibid.*, p. 643.

⁷⁰ G. B. Brown and V. du Vigneaud, *ibid.*, 1941, **141**, 85.

⁷¹ K. Hofmann, D. B. Melville, and V. du Vigneaud, *ibid.*, p. 207.

⁷² *Ibid.*, p. 620.

certain conditions a dietary essential for rats,⁷³ absence of it causing an excessive deposition of fat in the liver and hæmorrhages in the kidney;⁷⁴ it is needed also by poultry for the prevention of perosis.⁷⁵ It seems that choline is concerned in the organism in carrying out transmethylation. For this purpose it can be replaced either by methionine or by betaine: the more of the latter substances there are in the diet the less choline is needed. On the other hand the need for choline increases when there is increasing cystine (or fat) in the diet. Viewed from another angle, choline or betaine, as biological methylating agents, enable the animal to utilise homocystine in place of methionine.⁷⁶ There may be similar inter-relations between choline on the one hand and vitamin B₆, nicotinic acid, or other "B" vitamins on the other.^{72, 77} As yet there is no evidence whether choline (or its biological equivalents) is needed by man.

Anti-grey-hair factor (? *p*-aminobenzoic acid). Loss of pigmentation in the fur of rats kept on deficient diets had been noted by numerous investigators.⁷⁸ Work by A. F. Morgan *et al.*,⁷⁹ G. Lunde and H. Kringstad,⁸⁰ and J. J. Olsen *et al.*^{80a} made it clear that a hitherto unidentified vitamin was concerned in preventing this disorder. It has been shown that silver foxes, dogs and guinea pigs also are susceptible to the deficiency.⁸¹

S. Ansbacher⁸² claims to have identified *p*-aminobenzoic acid, previously recognised as a growth-promoting factor for plants, as the anti-grey-hair vitamin. Clinical applications for it have already been put forward,⁸³ but there is still a conflict of evidence whether *p*-aminobenzoic acid, or maybe

⁷³ C. H. Best, M. E. Huntsman, E. W. McHenry, and J. H. Ridout, *J. Physiol.*, 1935, **84**, 38.

⁷⁴ W. H. Griffith and N. J. Wade, *J. Biol. Chem.*, 1939, **131**, 567; B. Sure, *J. Nutrition*, 1940, **19**, 71; R. W. Engel and W. D. Salmon, *ibid.*, 1941, **22**, 109.

⁷⁵ O. D. Abbott and C. U. DeMasters, *ibid.*, 1940, **19**, 47; T. H. Jukes, *J. Biol. Chem.*, 1940, **134**, 789; *J. Nutrition*, 1940, **20**, 445; A. G. Hogan, L. R. Richardson, H. Patrick, and H. L. Kempster, *ibid.*, 1941, **21**, 327; *J. Biol. Chem.*, 1941, **138**, 459.

⁷⁶ J. P. Chandler and V. du Vigneaud, *ibid.*, 1940, **135**, 223; H. J. Channon, M. C. Manifold, and A. P. Platt, *Biochem. J.*, 1940, **34**, 866; A. D. Welch, *J. Biol. Chem.*, 1941, **137**, 173; H. P. Jacobi, C. A. Baumann, and W. J. Meek, *ibid.*, 1941, **138**, 571; W. H. Griffith, *J. Nutrition*, 1941, **21**, 291; W. H. Griffith and D. J. Mulford, *J. Amer. Chem. Soc.*, 1941, **63**, 929.

⁷⁷ P. György and R. E. Eckardt, *Biochem. J.*, 1940, **34**, 1143; P. György and H. Goldblatt, *J. Exp. Med.*, 1940, **72**, 1; W. H. Griffith and D. J. Mulford, *J. Nutrition*, 1941, **21**, 633; J. C. Forbes, *ibid.*, 1941, **22**, 359.

⁷⁸ For early literature, see A. Bakke, V. Aschehoug, and C. Zbinden, *Compt. rend. Acad. Sci. U.R.S.S.*, 1930, **191**, 1157; F. J. Gorter, *Nature*, 1934, **134**, 382; *Z. Vitaminforsch.*, 1935, **4**, 277; G. A. Hartwell, *Biochem. J.*, 1923, **17**, 547; P. György, *ibid.*, 1935, **29**, 741.

⁷⁹ A. F. Morgan, B. B. Cook, and H. G. Davison, *J. Nutrition*, 1938, **15**, 27.

⁸⁰ *Z. physiol. Chem.*, 1939, **257**, 201; *J. Nutrition*, 1940, **19**, 321.

^{80a} J. J. Oleson, C. A. Elvehjem, and E. B. Hart, *Proc. Soc. Exp. Biol. Med.*, 1939, **42**, 283.

⁸¹ G. Lunde and H. Kringstad, *Naturwiss.*, 1939, **27**, 755; A. F. Morgan and H. D. Simms, *J. Nutrition*, 1940, **20**, 627.

⁸² *Science*, 1941, **93**, 164.

⁸³ B. F. Sieve, *ibid.*, 1941, **94**, 257.

alternative factors—*e.g.*, biotin, pantothenic acid—do or do not in fact cure rats of their grey hairs.⁸⁴

Anti-alopecia Factor for Mice (? Inositol, Bios I).—Inositol, cyclohexane-hexol, has been known since 1928⁸⁵ to be a growth stimulant for yeast, classified as “bios I.” In 1940 D. W. Woolley,⁸⁶ by feeding mice on a restricted diet, produced in them a disease characterised by hairlessness of the trunk and cessation of growth. Later he stated that the protective substance was inositol.⁸⁷ Certain related substances, *e.g.*, inositol hexaacetate, cephalin, and phytic acid (inositol hexaphosphate), were found active.⁸⁸ We seem therefore to have the entertaining anomaly that, whereas small amounts of phytic acid act as a vitamin for mice, or as a growth stimulant for yeast, yet larger amounts act as a “toxamin” or “anti-vitamin.”⁸⁹

Folic Acid, Grass Juice Factor.—Folic acid, a substance necessary for the nutrition of yeast, occurs abundantly (as its name implies) in the leaves of plants. It has recently been isolated,⁹⁰ and its possible relation to the grass juice factor,⁹¹ needed by guinea pigs, still remains to be decided.

Classification of “Bios” Factors.—Since the various components of “bios” (the growth-promoting stimulant for yeast whose effects were first described in 1901⁹²) have lately been identified with certain vitamins needed by mammals, the following table of synonyms may help to remove confusion :

Bios	{	Bios I	= Inositol (? mouse anti-alopecia factor)
		Bios II {	IIA = Pantothenic acid (filtrate factor, $\gamma\gamma$ -dihydroxy- $\beta\beta$ -dimethylbutyryl- β -alanine)
			IIB = Biotin (vitamin H, co-enzyme R)

L. J. H.

2. THE METABOLISM OF NITROGENOUS COMPOUNDS.

Recent advances in our knowledge of the intermediary metabolism of nitrogenous compounds have been due mainly to the application of three different methods : (1) the study of nutritional requirements of animals (mainly non-ruminants) and the replacement of naturally occurring substances by related compounds, (2) the investigation of biochemical reactions catalysed by tissue slices, cell extracts and purified enzymes, (3) the use of “labelled” compounds, *i.e.*, substances containing heavy or radioactive

⁸⁴ K. Unna, G. V. Richards, and W. L. Sampson, *J. Nutrition*, 1941, **22**, 553; L. M. Henderson, J. M. McIntire, H. A. Waisman, and C. A. Elvehjem, *ibid.*, 1942, **23**, 47; R. R. Williams, *Science*, 1940, **92**, 561; P. György and C. E. Poling, *Proc. Soc. Exp. Biol. Med.*, 1940, **45**, 773.]

⁸⁵ E. V. Eastcott, *J. Physical Chem.*, 1928, **32**, 1094.

⁸⁶ *J. Biol. Chem.*, 1940, **136**, 113.

⁸⁷ D. W. Woolley, *Science*, 1940, **92**, 384; *J. Biol. Chem.*, 1941, **139**, 29.

⁸⁸ *Idem*, *ibid.*, 1941, **140**, 461.

⁸⁹ Cf. above, p. 234.

⁹⁰ H. K. Mitchell, E. E. Snell, and R. J. Williams, *J. Amer. Chem. Soc.*, 1941, **63**, 2284.

⁹¹ See *Ann. Reports*, 1940, **37**, 393.

⁹² E. Wildiers, *La Cellule*, 1901, **18**, 313.

isotopes. It is impossible to review the whole field adequately within the space available, but a few general problems may be discussed.

Essential Amino-acids.

It has been known for a considerable time that animals, with the possible exception of ruminants, require certain amino-acids in their diets. These "essential" amino-acids may be necessary for two purposes: they have to serve as the building material of the body proteins ("structural" requirements) and will therefore be particularly important for the growing animal, or may be needed for some specific chemical function ("functional" requirements). In some cases such a specific function is known, *e.g.*, arginine is necessary for the formation of creatine and methionine is needed as supplier of methyl groups. In other cases, however, a specific biochemical function can be inferred, although its precise nature may be still obscure. Valine deficiency, *e.g.*, leads to severe nervous symptoms in the rat,¹ from which it appears likely that this amino-acid is important for some specific biological reaction. The distinction between essential and non-essential amino-acids is, however, not very sharp. The absolutely non-essential amino-acids are mainly those which are related to keto-acids occurring in the metabolism of carbohydrates, such as glutamic and aspartic acids and alanine; other non-essential amino-acids are serine, proline and hydroxyproline. A second group of amino-acids consists of compounds which may be called "semi-essential"; thus arginine, although it is synthesised by the rat,² is not formed fast enough to permit optimal growth; ³ for the chick arginine is indispensable, since it cannot form it at all or only very slowly.⁴ Glycine also is not essential for the rat and is apparently necessary for optimal growth in the chick.⁵ Choline is another nitrogenous compound which is synthesised by animals ⁶ in amounts insufficient for metabolic requirements at least under certain dietary conditions.⁷ Another type of "semi-essential" amino-acid is only dispensable if a related essential amino-acid is provided in the diet in amounts sufficient to cover the requirements of both substances. Thus cystine, which can be made from methionine, is without growth effect if large amounts of methionine are fed; ⁸ cystine stimulates growth, however, if methionine is supplied in suboptimal amounts.⁹ A similar position may possibly exist for tyrosine and its relationship to phenylalanine.

The third group comprises the truly "essential" amino-acids, leucine, isoleucine, valine, threonine, histidine, lysine, phenylalanine, tryptophan

¹ W. C. Rose and S. H. Eppstein, *J. Biol. Chem.*, 1939, **127**, 677.

² C. W. Scull and W. C. Rose, *ibid.*, 1930, **89**, 109.

³ W. C. Rose, *Physiol. Rev.*, 1938, **18**, 109.

⁴ A. Arnold, O. L. Kline, C. A. Elvehjem, and E. B. Hart, *J. Biol. Chem.*, 1936, **116**, 699.

⁵ H. T. Almquist and E. Mecchi, *ibid.*, 1940, **135**, 355.

⁶ H. P. Jacoby, C. A. Baumann, and W. J. Meek, *ibid.*, 1941, **138**, 577.

⁷ See the review by W. J. Griffith, *J. Nutrition*, 1941, **22**, 239.

⁸ M. Womack, K. S. Kemmerer, and W. C. Rose, *J. Biol. Chem.*, 1937, **121**, 403.

⁹ M. Womack and W. C. Rose, *ibid.*, 1941, **141**, 375.

and methionine, which are indispensable for growth³ and cannot be made from substances normally present in animal diets. It has been claimed that all these nine amino-acids are also necessary for maintenance of nitrogen equilibrium in the adult;¹⁰ E. W. Burroughs, H. S. Burroughs, and H. H. Mitchell,¹¹ however, find that all the essential amino-acids are not equally important for maintenance; thus threonine and isoleucine occupy somewhat a key position, whilst lysine and histidine are considered non-essential for the adult rat. These authors also consider phenylalanine not essential for the adult if tyrosine is provided. The duration of these experiments seems, however, too short for such very definite conclusions to be drawn.

Investigations using Isotopes.

This particular field has been reviewed recently by R. Schoenheimer and D. Rittenberg¹² and only those results are discussed here which are of a very general character. If isotopic nitrogen is fed to rats in the form of ammonium salts,¹³ *l*(-)-leucine,¹⁴ *d*(+)-leucine,¹⁵ glycine¹⁶ or *dl*-tyrosine,¹⁷ a considerable part of the marked nitrogen is recovered from the tissue proteins. The isotopic nitrogen was found to be present in all amino-acids with the exception of lysine. The authors concluded that a rapid and extensive interchange of nitrogen takes place between dietary amino-acids and tissue proteins, involving the opening of peptide linkages, deamination, reamination or possibly transamination of amino-acid residues. It would follow that the old distinction between endogenous and exogenous nitrogen metabolism which is due to O. Folin¹⁸ must be abandoned. This old conception, which has recently been restated and defended,¹⁹ can certainly not be maintained in its original form, since it has been shown that a considerable fraction of the nitrogen of creatinine which was supposed to be a measure of the endogenous metabolism is provided by normal constituents of the food. There is, however, evidence that some proteins, such as the serum proteins, are metabolically more active than others, and there may even be some proteins which are completely inert.

This interchange between dietary nitrogen and the amino-acid residues bound in the tissue proteins is interpreted as involving the oxidative deamination of amino-acids to keto-acids and resynthesis. That such a formation of amino-acids from the corresponding keto-acids actually takes place is shown by the fact that most keto- and α -hydroxy-acids replace their corresponding essential amino-acids.²⁰ Lysine, however, cannot be replaced

¹⁰ P. A. Wolf and R. C. Corley, *Amer. J. Physiol.*, 1939, **127**, 589.

¹¹ *J. Nutrition*, 1940, **19**, 363, 385. ¹² *Physiol. Rev.*, 1940, **20**, 218.

¹³ G. L. Foster, R. Schoenheimer, and D. Rittenberg, *J. Biol. Chem.*, 1939, **127**, 319.

¹⁴ R. Schoenheimer, S. Ratner, and D. Rittenberg, *ibid.*, 1939, **130**, 703.

¹⁵ S. Ratner, R. Schoenheimer, and D. Rittenberg, *ibid.*, 1940, **134**, 653.

¹⁶ D. Rittenberg, R. Schoenheimer, and A. S. Keston, *ibid.*, 1939, **128**, 319.

¹⁷ R. Schoenheimer, S. Ratner, and D. Rittenberg, *ibid.*, 1939, **127**, 333.

¹⁸ *Amer. J. Physiol.*, 1905, **13**, 117.

¹⁹ E. W. Burroughs, H. S. Burroughs, and H. H. Mitchell, *J. Nutrition*, 1940, **19**, 271.

²⁰ W. C. Rose, *Physiol. Rev.*, 1938, **18**, 109.

by α -hydroxy- ϵ -aminohexanoic acid;²¹ this fact is in accordance with the results obtained with the use of isotopes,²² which shows that for lysine deamination is irreversible. The availability of the hydroxy- or keto-acid analogue of threonine has not been examined.

D-Amino-acids can be deaminated *in vitro* by the *D*-amino-acid oxidase; it is therefore to be expected that all essential *L*-amino-acids which can be replaced by their corresponding keto-acids should also be replaceable by their *D*-isomerides. This is actually the case for histidine, tryptophan, phenylalanine and methionine; *L*-leucine, *L*-isoleucine and *L*-valine cannot, however, be replaced by the *D*-compounds,²⁰ although *in vitro* experiments indicate a fairly high rate of deamination.²³ The reason for this discrepancy is quite obscure.

The observation that phenylalanine can cover the dietary requirements of both phenylalanine and tyrosine for the growing animal must mean that phenylalanine can be converted into tyrosine and that the reaction is irreversible. This interpretation was confirmed by A. R. Moss and R. Schoenheimer,²⁴ who fed *DL*-deuterophenylalanine to rats and recovered isotopic tyrosine from the tissue proteins. The conversion of hydroxy-acids into the corresponding amino-acids which follows from the feeding experiments mentioned has also been demonstrated directly by feeding deuterio-*DL*- β -phenyl-lactic acid and the recovery of labelled tyrosine.²⁵

The special function which a particular amino-acid may have to serve has been very clearly demonstrated in the case of methionine. This amino-acid is necessary to build up the tissue proteins and it can replace—as mentioned above—cystine. H. Tarver and C. L. A. Schmidt²⁶ have investigated the fate of methionine containing radioactive sulphur and were able to show the presence of isotopic sulphur in the cystine isolated from the tissues. But the most interesting function of methionine is probably its ability to supply methyl groups for two important biosyntheses, the formation of choline and creatine.

Choline Metabolism.

It has been known for some time that dietary choline can prevent the accumulation of fats in the livers of animals fed on certain diets.²⁷ It was noticed later that methionine has a similar "lipotropic" effect,²⁸ whereas cystine produces an increase in the deposition of liver fat.²⁹ In the meantime, evidence of the inter-relationship between choline and methionine was obtained by du Vigneaud and his co-workers. They demonstrated that homocystine and homocysteine are incapable of supporting growth of animals

²¹ O. A. McGinty, H. B. Lewis, and C. S. Marvel, *J. Biol. Chem.*, 1924, **62**, 75.

²² N. Weissman and R. Schoenheimer, *ibid.*, 1941, **140**, 779.

²³ H. A. Krebs, *Biochem. J.*, 1935, **29**, 1620.

²⁴ *J. Biol. Chem.*, 1940, **135**, 415.

²⁵ A. R. Moss, *ibid.*, 1940, **137**, 739.

²⁶ *Ibid.*, 1939, **130**, 67.

²⁷ C. H. Best and T. M. Hershey, *J. Physiol.*, 1932, **75**, 56.

²⁸ H. F. Tucker and H. C. Eckstein, *J. Biol. Chem.*, 1937, **121**, 479.

²⁹ H. J. Channon, M. C. Manifold, and A. P. Platt, *Biochem. J.*, 1938, **32**, 969;
A. W. Beeston and H. J. Channon, *ibid.*, 1938, **30**, 280.

on a diet devoid of cystine and methionine; administration of choline, however, enables the animal to utilise homocystine instead of methionine.³⁰ The conclusions drawn from these experiments that methyl groups can be transferred reversibly between methionine and choline and that the presence of donors of labile methyl groups is essential in diets, have been confirmed by later work using labelled methyl groups. If methionine containing a deuteromethyl group is fed to rats, choline containing a high concentration of deuterium in its methyl groups can be isolated from the tissues.³¹

Choline deficiency may also lead to a severe hæmorrhagic renal degeneration,³² which can be prevented by choline, methionine and betaine³³ and is aggravated by cystine and cholesterol.³⁴

Creatine Metabolism.

H. Borsook and J. W. Dubnoff³⁵ showed that guanidoacetic acid was slowly converted by tissue slices into creatine and that methionine alone of many substances tested increased greatly the rate of this reaction. The actual transfer of the methyl group from methionine to creatine *in vivo* was later clearly demonstrated by du Vigneaud *et al.*³¹ with the aid of labelled methyl groups. Guanidoacetic acid is formed in the body mainly from arginine and glycine,³⁶ but other nitrogenous substances act only as potential precursors of creatine in so far as their nitrogen is utilised for the synthesis of glycine and arginine. It could also be shown that arginine provides the amidine part of the molecule, and glycine supplies the sarcosine moiety. The shift of methyl groups which is demonstrated by all these investigations is, however, not completely reversible. Methyl groups are interchangeable between choline and methionine and both choline and methionine can function as methyl donors to creatine. The latter reaction appears, however, to be irreversible.³⁷

A. N.

3. THE MECHANISM OF MUSCLE CONTRACTION.

Knowledge of the nature of the protein myosin, of which the contractile muscle fibril is composed, has been greatly extended during the last few years. K. Bailey¹ and J. G. Sharp² have studied the amino-acid content of myosin. Bailey estimated the cystine, methionine, tyrosine and tryptophan, and Sharp the basic amino-acids, dicarboxylic acids and mono-amino-acids, with the result that 85% of the protein is now identified.

³⁰ V. du Vigneaud, J. P. Chandler, A. W. Moyer, and D. M. Keppel, *J. Biol. Chem.*, 1939, **131**, 57.

³¹ V. du Vigneaud, M. Cohn, J. P. Chandler, J. R. Schenck, and S. Simmonds, *ibid.*, 1941, **140**, 625.

³² W. H. Griffith and N. J. Wade, *ibid.*, 1939, **131**, 567.

³³ W. H. Griffith, *J. Nutrition*, 1941, **21**, 291.

³⁴ W. H. Griffith and O. J. Mulford, *ibid.*, p. 633.

³⁵ *J. Biol. Chem.*, 1940, **132**, 559.

³⁶ K. Bloch and R. Schoenheimer, *ibid.*, 1941, **138**, 167.

³⁷ V. du Vigneaud, J. P. Chandler, and A. W. Moyer, *ibid.*, 1941, **139**, 917.

¹ *Biochem. J.* 1937, **31**, 1406.

² *Ibid.*, 1939, **33**, 679.

Myosin contains very little cystine sulphur, most of the sulphur being in the form of methionine; some of the cystine is present in the reduced --SH form even in native myosin and the effect of various treatments upon the --SH content has been much studied.^{3,4,5} W. T. Astbury and S. Dickinson⁶ have made an important X-ray and elastic study of strips of myosin film, made by drying the sol, and prepared in such a way that the myosin chain molecules are oriented. When oriented but unstretched, they give an α -photograph, almost indistinguishable from that of α -keratin; when stretched, they give a β -photograph. The X-ray and elastic properties of myosin resemble those of keratin that has suffered breakdown among the cross linkages, including S—S bridges, of the polypeptide grid, *i.e.*, the super-contracting form of keratin. Quantitative study by means of X-rays of the structural changes accompanying super-contraction of myosin films shows that the effect must be due to further regular folding of the polypeptide chains, and cannot be due merely to disorientation of long thin units. The hypothesis is put forward that muscle contraction arises from super-contraction of its myosin component. Astbury^{7,8} has suggested a new view of the nature of the intramolecular fold in α -keratin and α -myosin; in the transformation from the flat polypeptide grid to the new α -configuration, all the experimental and structural conditions are satisfied, in particular, space is available for the side-chains standing out alternately on one side and the other of the plane of the fold.

In view of the structural importance of myosin, it is of very great interest to learn that enzyme properties are also associated with this protein, especially as this enzyme activity consists precisely in bringing about that reaction (the hydrolysis of adenosine triphosphate, henceforward referred to as ATP) which has for some time past been recognised as the chemical change providing the energy for the muscle contraction. V. A. Engelhardt and M. N. Ljubimova⁹ and Ljubimova and Engelhardt¹⁰ first showed that adenosine triphosphatase activity is associated with the myosin fraction of the muscle proteins; when the myosin is purified by several precipitations, the power (shown by muscle brei and less purified myosin) to split off the second phosphate group is lost. The action of the myosin thus consists in splitting off one phosphate group from ATP with formation of adenosine diphosphate (ADP). These fundamental observations have been confirmed and extended by workers in several laboratories.^{11, 12, 13, 14, 14a} Bailey¹⁴

³ A. T. Todrick and F. Walker, *ibid.*, 1937, **31**, 392.

⁴ J. P. Greenstein and J. Edsall, *J. Biol. Chem.*, 1940, **133**, 397.

⁵ A. E. Mirsky, *J. Gen. Physiol.*, 1936, **19**, 559.

⁶ *Proc. Roy. Soc.*, 1940, B, **129**, 307.

⁷ *Nature*, 1941, **147**, 696.

⁸ *Chem. and Ind.*, 1941, **60**, 491.

⁹ *Nature*, 1939, **144**, 668.

¹⁰ *Biochimia*, 1939, **4**, 716.

¹¹ M. N. Ljubimova and D. Pevsner, *ibid.*, 1941, **6**, 178.

¹² A. Szent-Györgyi, and I. Banga, *Science*, 1941, **93**, 158.

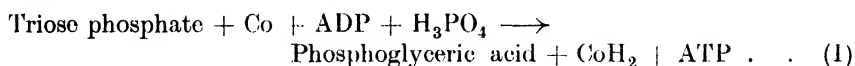
¹³ J. Needham, S. C. Shen, D. M. Needham, and A. S. C. Lawrence, *Nature*, 1941, **147**, 766.

¹⁴ K. Bailey, in the press.

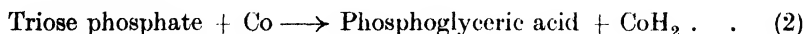
^{14a} D. M. Needham, in the press.

has studied the kinetics and specificity of the reaction, and its activation by metallic ions, of which Ca^{++} is the most efficient. Needham, Shen, Needham, and Lawrence¹³ found a large reversible fall in flow birefringence when ATP was added to myosin sol. This large effect, specific for ATP amongst many substances tried, may indicate a combination between the myosin and the ATP, such as might be expected between enzyme and substrate.

When the stimulus to contraction reaches the muscle fibril, the immediate change providing energy seems to be the breakdown of ATP with formation of ADP and inorganic phosphate. (It is at present uncertain whether this breakdown is simultaneous with the shortening of the fibrils, or whether it is the first of the " recovery processes " bringing about lengthening and " recharging " of the contracted fibrils.) It is well known that the ATP thus broken down is built up again by three distinct processes : (a) by reaction with creatine phosphate ; (b) by reaction with phosphopyruvate ; (c) by esterification of phosphate coupled with the oxido-reduction between triose phosphate and pyruvate. The nature of the last process has recently been elucidated by O. Warburg and W. Christian.¹⁵ It had been shown^{16, 17, 18, 19} that the part of this oxido-reduction essential for the esterification is the reaction between triose phosphate and co-enzyme I :



D. M. Needham and R. K. Pillai,²⁰ using extracts of muscle acetone powder, had shown that arsenate affects the course of the reactions in that the oxido-reduction continues in its presence while the disappearance of inorganic phosphate and the formation of ATP is prevented. Meyerhof *et al.*,¹⁹ using more purified enzyme preparations from yeast, had shown that the reaction between triose phosphate and co-enzyme alone proceeds only slowly and soon stops. The reaction goes further if ADP and inorganic phosphate are present, and practically to completion if glucose is also present. Meyerhof *et al.*^{19, 21} had recognised that the whole process (equation 1) is reversible ; further, they had found that in presence of arsenate, even in absence of ADP, the reaction between triose phosphate and co-enzyme goes to completion



E. Adler and G. Günther,²² using partly purified preparations from brain and yeast, had also drawn attention to the fact that this reaction (2) comes to a standstill before the reactants are exhausted, as if at an equilibrium

¹⁵ *Biochem. Z.*, 1939, **303**, 40.

¹⁶ D. M. Needham and R. K. Pillai, *Biochem. J.*, 1937, **31**, 1837.

¹⁷ O. Meyerhof, W. Schulz, and P. Schuster, *Biochem. Z.*, 1937, **293**, 309.

¹⁸ D. M. Needham and G. D. Lu, *Biochem. J.*, 1938, **32**, 2040.

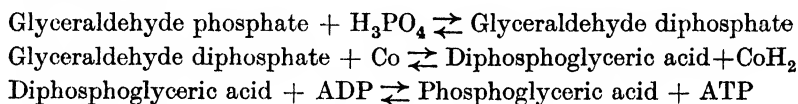
¹⁹ O. Meyerhof, P. Ohlmeyer, and W. Möhle, *Biochem. Z.*, 1938, **297**, 90.

²⁰ *Nature*, 1937, **140**, 165.

²¹ O. Meyerhof, P. Ohlmeyer, and W. Möhle, *Biochem. Z.*, 1938, **297**, 193.

²² *Z. physiol. Chem.*, 1938, **253**, 153.

point. This equilibrium, however, cannot be altered by adding phosphoglyceric acid, and they had concluded that an unknown intermediate must be involved. They also had found an effect of arsenate, which caused the reaction to go rapidly to completion. Warburg and Christian were able to link together and explain all these facts. They obtained from yeast a pure crystalline preparation of the enzyme responsible for the oxidation of glyceraldehyde phosphate by co-enzyme. Like Adler and Günther, they observed an apparent equilibrium point not affected by addition of phosphoglyceric acid, and in presence of arsenate the reaction went to completion. They observed also that, in absence of arsenate, phosphate is necessary for the reaction, and phosphate concentration affects the equilibrium point. These observations led to the isolation by E. Negelein and H. Brömel²³ of the intermediate 1 : 3-diphosphoglyceric acid. Further, by addition of another specific enzyme preparation to the crystalline triose phosphate dehydrogenase, a system was obtained which could transfer phosphate from the diphosphoglyceric acid formed to ADP. The series of reactions involved in the coupled phosphorylation of ADP may therefore be formulated thus :



The effect of arsenate is explained by Warburg and Christian in the following way. Arsenate can replace phosphate in the reaction and an arsenylated glyceraldehyde phosphate is formed and oxidised; the arsenylated phosphoglyceric acid is, however, unlike the diphosphoglyceric acid, unstable under the experimental conditions, and breaks down irreversibly. 1 : 3-Diphosphoglyceric acid thus takes its place with creatine phosphate and phosphopyruvic acid in the chemistry of muscle contraction as one of the sources of energy and of phosphate for the reconstitution of ATP. The whole subject of the importance of the guanidine phosphate, enol phosphate and carboxyl phosphate groupings for transfer of energy has been considered by H. Kalckar.²⁴

D. M. N.

4. PHYSICOCHEMICAL PHENOMENA.

Intracellular Gels and Studies on Gel-forming Systems of the Cytoplasm.

In the last two or three decades many interesting studies were made on gelatin sols and gels. These studies have been profitable from a physicochemical point of view but, except in the most abstract manner, have not contributed to our knowledge of the part played by gels in biological systems. For this there are two causes : gelatin is not, so far as we know, one of the substances responsible for intracellular gelation; nor has the information available on the cytological level made it at all plain, until quite recently, what

²³ *Biochem. Z.*, 1939, **303**, 231.

²⁴ *Chem. Reviews*, 1941, **28**, 71; *Biol. Rev.*, 1941 **17**, 28.

importance must be attached to intracellular gels, or from what point of view the intracellular gels may most profitably be studied. In the last five or ten years there has been a substantial increase in our knowledge of the function of gels in cells, and also a growing volume of work on the properties of myosin, the chief gel-forming substance in muscle cells.

Micro-dissection¹ has made a most useful contribution by demonstrating that the cortical cytoplasmic layer of many cells is gelled and that in the resting cell the bulk of the remaining part of the cytoplasm is comparatively fluid. The asters, spindle and chromosomes of dividing cells are gelled elastic bodies, and in some instances are known to be birefringent.² One of the most valuable results is that of E. N. Harvey and D. A. Marsland,³ who observed cells through the microscope during the process of centrifugation. They found that, even in the "fluid" part of the cytoplasm, intracellular particles may move in an intermittent fashion under centrifugal force; this is an indication that even the fluid part of the cytoplasm may be weakly gelled or undergo intermittent sol \rightleftharpoons gel transformations. These various observations have made it certain that gels exist in living cells, and that many of the observable bodies in the interior of cells are elastic gels: from birefringence studies it has been concluded that many of these bodies consist of adlineated needle-shaped protein particles.² Some of these gels are known to be thixotropic.¹

The importance of these observations on the physicochemical condition of the interior of the cell has been emphasised by a series of studies on the effect of moderately high pressure on cells. Earlier work in this field has been reviewed by McK. Cattell.⁴ The important feature of more recent work is the demonstration that in a wide variety of cell types the application of pressure reduces the cytoplasmic viscosity and eventually liquefies the cortical gel layer. The liquefaction usually occurs at a pressure of the order of 400 atms.; it is followed immediately by profound changes in behaviour. Cells of irregular shape round up into spheres,⁵ long tentacles break up under surface tension forces into a string of spherical droplets,⁶ protoplasmic streaming ceases,⁷ and dividing cells which have reached the "dumbell" stage revert to the spherical state.⁸ The liquefaction of the gel is reversible. For each increment of 68 atms. pressure a number of cell characteristics were found to be diminished to 0.76 of their former value. This is true of the cytoplasmic viscosity of ova of two species of *Arbacia*, the viscosity of two species of *Amoeba* and of the leaf cells of *Elodea*; the rate of impingement of the cleavage furrow on the division axis in two species of *Arbacia*; and the velocity of protoplasmic streaming in *Elodea*. The view has been advanced that the liquefaction of the gels is due to hydration of protein molecules; but, as

¹ R. Chambers, 1924, in "General Cytology," Ed. Cowdray, Chicago; *J. Cell. Comp. Physiol.*, 1938, **12**, 149.

² L. E. R. Picken, *Biol. Rev.*, 1940, **15**, 133.

³ *J. Cell. Comp. Physiol.*, 1932, **2**, 75.

⁴ *Biol. Rev.*, 1936, **11**, 485.

⁵ D. A. Marsland and D. E. S. Brown, *J. Cell. Comp. Physiol.*, 1936, **8**, 167, 171.

⁶ J. A. Kitching and D. C. Pease, *ibid.*, 1939, **14**, 133.

⁷ D. A. Marsland, *ibid.*, 1938, **12**, 57.

⁸ D. A. Marsland, *ibid.*, 1939, **13**, 15, 23.

Cattell remarks, at present the possibility has not been eliminated that "the changes in viscosity are secondary to changes resulting from stimulation or chemical reactions."⁴ It is known that even globular proteins such as ovalbumin, serum albumin and insulin form thixotropic gels and show anisotropy of flow when denatured, or when their SS bonds are reduced to SH.⁹ Whatever the explanation of these changes may be, it is now clear that sol \rightleftharpoons gel changes play an essential rôle in cell behaviour, and that physicochemical studies on the molecules concerned in these changes are of great interest. These studies have so far been restricted, with few exceptions, to observations on myosin, the protein forming the spontaneously birefringent gel of muscle fibres.* Several observers¹⁰ have found that when a muscle passes into rigor a large part of the myosin is no longer soluble in potassium chloride solution. A. E. Mirsky^{11, 12, 13} has investigated the nature of this change and its relation to muscular activity. When the thixotropic gel formed by native (soluble) frog myosin is heated to 38—39°, its solubility is lost. The Q_{10} for this reaction is about 1,000. There is little change in the SH groups. A small diminution in transparency of the gel occurs. If the temperature is raised further (41—45°), the gel-structure is destroyed, opaque clumps forming, and SH groups appearing. The reaction resulting in appearance of SH groups has a much lower Q_{10} than the reaction producing insolubility. With previously studied proteins these two steps (loss of solubility and appearance of SH groups) appear to be more closely linked than with myosin. Physiological processes corresponding to these changes are thermal (reversible) shortening of frog muscle,^{14, 15} which has a sudden onset at 38°. This thermal contracture, which Mirsky considers to be due to the first step in myosin denaturation (loss of solubility), is of the same order of magnitude as the contraction in an electrically produced tetanus. A further shortening occurs when the muscle is heated from 39° to 45°; this process is irreversible and is regarded by Mirsky as due to the change in insoluble myosin which is accompanied by appearance of SH groups.

In vitro the initial denaturation change (loss of solubility) may also be produced by simple physical means, such as dehydration by cold and by substances such as caffeine, nicotine, chloroform and glycocholate. Veratrine does not initiate or accelerate denaturation. This may be regarded as strong evidence for the view that the initial stage of denaturation is involved in muscular contraction, for the first group of substances throw a muscle into

⁹ W. G. Myers, *Cold Spring Harbor Symposium*, 1938, **6**, 120; H. Neurath, *ibid.*, p. 118; C. Stern, *ibid.*, p. 119; A. White, *ibid.*, p. 265.

¹⁰ P. Saxl, *Beitr. Chem. Physiol.*, 1907, **9**, 1; A. E. Mirsky, *J. Gen. Physiol.*, 1935, **19**, 571; E. B. Smith, *Proc. Roy. Soc.*, 1937, *B*, **124**, 136.

¹¹ *J. Gen. Physiol.*, 1937, **20**, 455.

¹² *Ibid.*, p. 461.

¹³ *Cold Spring Harbor Symposium*, 1938, **6**, 153.

¹⁴ E. Gottschlich, *Pflügers Arch.*, 1893, **54**, 109; **55**, 339.

¹⁵ P. Jensen, *ibid.*, 1914, **160**, 333.

* The physical chemistry of the gels of the nucleus has had some slight attention, but not sufficient for discussion here.

a reversible contracture¹⁶ (sustained single contraction), whereas veratrine produces a similar result, but by acting on the nervous system to give a tetanus¹⁷ (many consecutive twitches).

A similar change in solubility after activity has been demonstrated in the myosin of crab limb muscle,¹⁸ and in a myosin-like protein found in sea-urchin eggs.¹⁹

A second approach to the subject has been made by Needham *et al.*,²⁰ who have endeavoured to link the phosphorylation cycles, whereby it is now believed that the energy obtained from carbohydrate oxidation is transferred to the contractile apparatus of the muscle, with the long-established fall in birefringence of a muscle occurring during contraction. It had previously been shown by A. Muralt and J. T. Edsall²¹ that myosin solution shows double refraction of flow. More recently W. A. Engelhardt and M. N. Ljubimova²² have found that myosin is so closely associated with the enzyme adenylypyrophosphatase that it is possible that myosin is itself the enzyme. As the breakdown of adenylypyrophosphate is believed to be the nearest in time to contraction of the known chemical processes occurring in active muscle, studies were made of the effect of adenylypyrophosphate on the flow birefringence of myosin. These experiments were carried out with a sol containing about 3% of myosin in 0.75M-potassium chloride and other solutions of equivalent ionic strength at p_H 7. Adenylypyrophosphate causes a large and prolonged fall in birefringence, which occurs in less than one minute at about 18° and takes considerably longer at 0°. This change is reversible. The birefringence returns to its original value in about two hours at 37°, and more slowly at lower temperatures.

This observation may well prove to be a key to the connection between muscle intermediary metabolism and the transformation of energy into mechanical work, especially if it proves possible to combine studies of viscosity and birefringence with X-ray studies. W. T. Astbury and S. Dickinson²³ have now shown that a process occurs in muscle protein during contraction which is closely analogous to supercontraction of keratin in which the cross-linkages of adjacent polypeptide chains of keratin have been broken by reduction of SS bonds: observation of the occurrence of such processes in relation to the action of adenylypyrophosphate would clinch the argument that this *in vitro* action of adenylypyrophosphate is closely analogous to the processes occurring in living muscle. In addition, X-ray studies are probably essential for making a detailed analysis of the action of adenylypyrophosphate,

¹⁶ K. J. A. Secher, *Arch. exp. Path. Pharm.*, 1914, **77**, 83; H. N. Langley, *J. Physiol.*, 1907, **36**, 347; G. Schwenker, *Pflügers Arch.*, 1914, **157**, 443.

¹⁷ G. Lamm, *Z. Biol.*, 1911, **56**, 223; 1912, **58**, 37.

¹⁸ J. F. Danielli, *J. Physiol.*, 1938, **92**, 3P.

¹⁹ A. E. Mirsky, *Science*, 1936, **84**, 333.

²⁰ J. Needham, S. C. Shen, D. M. Needham, and A. S. C. Lawrence, *Nature*, 1941, **147**, 766.

²¹ *J. Biol. Chem.*, 1930, **89**, 315, 351.

²² *Nature*, 1939, **144**, 668; *Biochimia*, 1939, **4**, 716; A. Szent-Györgi and I. Bang, *Science*, 1941, **93**, 158.

²³ *Proc. Roy. Soc.*, 1940, B, **129**, 307.

for this probably cannot be achieved from studies of viscosity and double refraction only.

Other studies of the action of ions on myosin flow birefringence have been made by Edsall and his colleagues.²⁴ The properties of threads of gelled myosin have also received attention.²⁵

All of the studies so far reported have, implicitly or explicitly, left the problem of intermicellar forces untouched. Since myosin in the muscle fibre is gelled, these forces must be of significant magnitude, and it may be that their study will enable a connection to be established between the response of a muscle fibre to a stimulus, and the observed changes in myosin birefringence and X-ray scattering during contraction: this connection is at present quite obscure. Important theoretical studies of intermicellar forces have been made by Langmuir and Levene.²⁶

J. F. D.

5. SOME PLANT PRODUCTS AND ENZYMES.

With the advent of the United States as a full belligerent, the diminution in the number of publications observable in recent months will doubtless become more marked. There appears to be no major development in plant biochemistry during the past year, but steady advances in knowledge have been maintained. The plant growth substances are amongst the most interesting and important of plant products. In this field, following the preparation of crystalline biotin, the constitution of this somewhat elusive member of the bios group is likely to be determined in the near future. Knowledge of the chemistry of the hydrolytic enzymes has lagged behind that of those enzymes concerned in oxidation and allied processes. The isolation in the crystalline state of increasing numbers of the former and the study of the properties of the pure enzymes are leading steadily to more complete understanding. These topics, together with some notes on plant proteins, are discussed in the following pages.

Growth Substances.—A concise review of growth substances in their practical and commercial aspects is contributed by M. A. H. Tincker.¹ The methods of detection and estimation of growth substances are undergoing continuous modification and elaboration; but a tendency is also to be noted towards simplification. Thus, the *Avena* method of auxin determination requires elaborate apparatus and technique not readily available to many workers. An upright-growth method which can be applied to cut pea shoots is described by E. G. Brain,² who has found it of value in comparative experiments under ordinary greenhouse conditions,

²⁴ J. P. Greenstein and J. T. Edsall, *J. Biol. Chem.*, 1940, **133**, 397; J. T. Edsall and J. W. Mehl, *ibid.*, p. 409.

²⁵ H. H. Weber and K. Meyer, *Biochem. Z.*, 1933, **266**, 137; H. H. Weber, *Pflügers Arch.*, 1935, **235**, 205; W. A. Engelhardt, M. N. Ljubimova, and R. A. Meitina, *Compt. rend. U.R.S.S.*, 1941, **30**, 644.

²⁶ I. Langmuir, *J. Chem. Physics*, 1938, **6**, 873; S. Levene, *Proc. Roy. Soc.*, 1939, **A**, **170**, 145.

¹ *Nature*, 1941, **147**, 439.

² *Ibid.*, 1941, **148**, 666.

and although not as exact as the more refined methods there are indications that its accuracy may be increased as the result of further experiments.

G. E. Turfitt³ has described a rapid method of testing substances for phytohormone activity, using yeast growth as the criterion, such growth being assessed by multiplication rates based on cell counts. β -Indolyl-, α - and β -naphthyl-, and phenyl-acetic acids in concentrations of $\frac{1}{10}$ to 1 part per million cause varying degrees of stimulation; further increases in concentration may cause a diminution or even inhibition of growth. As no stimulation is observable with washed yeast, it is thought that the action of substances such as those mentioned is combined with that of the bios substances, which would be removed by washing.

Experiments by E. J. Kraus and J. W. Mitchell,^{4, 5} on bean plants, which showed characteristic responses, indicate that α -naphthylacetamide may be added to the extending list of plant growth substances. Treatment on cut stems was carried out with the compound in lanolin, or in aqueous emulsion with lanolin; seedlings were also sprayed.

The wound hormone, traumatic acid, which promotes wound periderm formation in potato, has been shown to be Δ^1 -decene-1:10-dicarboxylic acid and it is of interest to enquire whether acids of the same general type are equally effective. J. English⁶ has prepared by synthesis a number of analogues of the acid of the general type $\text{CO}_2\text{H} \cdot [\text{CH}_2]_n \cdot \text{CH} \cdot \text{CH} \cdot \text{CO}_2\text{H}$ and $\text{CO}_2\text{H} \cdot [\text{CH}_2]_n \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CO}_2\text{H}$. Δ^5 -Undecene-1:11-dicarboxylic acid and $\Delta^{1:7}$ -octadiene-1:8-dicarboxylic acid were also prepared and examined. All the acids thus synthesised were found to be active plant wound hormones.

Bios.—As indicated in last year's *Annual Reports*,⁷ it has been suggested that biotin is identical with vitamin H, a substance which protects rats from "egg-white injury." Full confirmation of the identity appears to be forthcoming as the result of experiments which demonstrated that the activity of the vitamin in stimulating yeast growth is identical with that of bios, and conversely that biotin may be used to remedy deficiency of the vitamin in rats. These confirmatory results were obtained by V. du Vigneaud, D. B. Melville, P. György, and C. S. Rose.⁸ It is also probable that coenzyme R, a growth factor for many strains of legume nodule bacteria, is identical with biotin and vitamin H (see also this vol., p. 235).

The isolation of biotin as the free acid rather than the ester marks a considerable step forward, since not only is it desirable in some biological investigations to employ the free acid, but a line of chemical attack on constitution has been opened up. The isolation of the free acid in crystalline form is described by V. du Vigneaud, K. Hofmann, D. B. Melville, and J. R. Rachele.⁹ The empirical formula ascribed to it is $\text{C}_{10}\text{H}_{16}\text{O}_3\text{N}_2\text{S}$, and titration curves indicate that the compound is a monocarboxylic acid. There is no specific absorption in the ultra-violet.

³ *Biochem. J.*, 1941, **35**, 237.

⁴ *Bot. Gaz.*, 1939, **101**, 204.

⁵ J. W. Mitchell and W. S. Stewart, *ibid.*, p. 410.

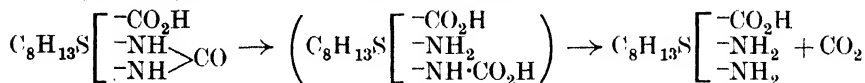
⁶ *J. Amer. Chem. Soc.*, 1941, **63**, 941.

⁷ *Ann. Reports*, 1940, **37**, 393.

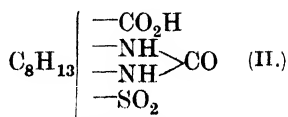
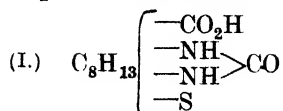
⁸ *Science*, 1940, **92**, 62.

⁹ *J. Biol. Chem.*, 1941, **140**, 763.

Using the crystalline preparation above, G. B. Brown and V. du Vigneaud¹⁰ have studied the stability of biotin towards a variety of reagents and treatments, employing yeast growth as a criterion of activity. It has been found that alkali or acid treatment results in inactivation, and that, whilst biotin is inactivated by many reagents which react with α -amino-acids, it is not affected by ninhydrin, a fact held to indicate strongly that biotin is not an α -amino-acid. Acylating, alkylating and carbonyl reagents do not inactivate biotin. Aeration under various conditions with air or oxygen has no effect, but activity is rapidly lost under the action of stronger oxidising agents such as hydrogen peroxide or bromine water; it is concluded that biotin contains an easily oxidisable group or groups. These experiments on activation have led to a direct chemical attack on the crystalline biotin with a view to disclosing the nature of the functional groups present in the molecule. The conclusion arrived at in the previous communication, that no α -amino-groups are present in the molecule, is confirmed by K. Hofmann, D. B. Melville, and V. du Vigneaud;¹¹ no nitrogen is produced when biotin is treated with nitrous acid by the van Slyke method, and the ninhydrin reaction is negative. Treatment of biotin with baryta at 140° for 20 hours led to the isolation as sulphate of a "diaminocarboxylic acid," $C_8H_{18}O_2N_2S$, which gave a dibenzoyl derivative, contained two free amino-groups and must have been derived from the parent biotin with the loss of one carbon and one oxygen atom. The most likely explanation of such a change suggests that a cleavage of a cyclic urea derivative is involved as below:



The nature of the sulphur atom was indicated as follows: Biotin contains no alkali-labile sulphur and does not liberate hydrogen sulphide when treated with zinc dust and hydrochloric acid. Further, no positive nitroprusside test could be obtained in presence or absence of sodium cyanide. The stability of the sulphur therefore indicates a probable thioether structure and experimental evidence supports this. Thus, biotin (I) on treatment with hydrogen peroxide and glacial acetic acid gives a crystalline sulphone (II) in 90% yield. There is no loss of carbon or hydrogen involved in the change, but two oxygen atoms are added. The production of a strong yellow colour when biotin and the diamino-carboxylic acid are treated with tetranitromethane, and the failure to produce a colour when the oxidation product is similarly treated, are also consonant with the suggestion that a thioether structure is involved. At this stage, then, the authors conclude that biotin is a carboxylic acid containing an *NN'*-substituted cyclic urea grouping, and sulphur in thioether linkage.



¹⁰ *J. Biol. Chem.*, 1941, **141**, 85.

¹¹ *Ibid.*, p. 207.

M. J. Pelczar, jun., and J. R. Porter¹² have shown that pantothenic acid is one of the growth factors for *Proteus morganii*, and in a later paper¹³ observe that this organism is specially suitable for the biological assay of pantothenic acid in natural materials. The response of the organism to pantothenic acid is extremely sensitive and specific, since 0.0002 µg. of the calcium salt is sufficient to initiate visible growth. In a number of tests the amounts indicated by the result of the assay corresponded closely with the amounts known to be present. The extreme sensitivity of the organism renders it specially suitable for dealing with small amounts of the material to be examined.

Methods of estimation of inositol involving isolation of the product from the material under investigation have not proved satisfactory, and moreover are unsuitable when dealing with small quantities. D. W. Woolley¹⁴ has developed a method of estimation based on the growth response of yeast to the presence of inositol in a medium which in its absence supported practically no growth. Graded amounts of inositol were found to induce graded responses, such growth being measured by a turbidimetric method. Quantitative results were obtained with a number of natural products. D. W. Woolley¹⁵ has also studied the biological specificity of *meso*-inositol in respect of mice and of yeast, and shown that in the latter case such specificity is virtually absolute. Thus for yeast, the following substances are inactive: *d*-inositol, *l*-inositol, pinitol, quebrachitol and quercitol; inositol hexa-acetate, phytin and soy bean cephalin; quinic acid and inosose. Mono- and tetra-phosphates of inositol were only 5 and 2% respectively as potent for yeast as inositol, and mytilitol (probably methyl inositol) had about one-tenth of the activity of inositol.

Additions to the list of growth factors for lower organisms are still forthcoming. Thus, following the observation of E. E. Snell and W. H. Peterson¹⁶ that there existed a new growth factor, probably a purine, for *Lactobacillus casei*, E. L. R. Stakstad¹⁷ reports the isolation of a dinucleotide or mixture of nucleotides from solubilised liver. This was obtained by adsorption on norit, followed by elution with a dilute solution of ammonia in 70% methanol. The product was purified until no increase in activity could be observed. It had the properties of a nucleotide, since it contained nitrogen, phosphorus and a pentose (not deoxyribose). Hydrolysis showed that the factor contained a purine and a pyrimidine nucleotide, the purine base being guanine, the pyrimidine base still awaiting identification. The "dinucleotide" may be partially replaced by guanine and thymine, and the former could be effectively replaced by adenine, hypoxanthine and xanthine. Uracil or cytosine could not replace thymine. This work is in line with that of E. E. Snell and H. K. Mitchell,¹⁸ who have found that both purine and pyrimidine bases are essential factors in the growth of *Lactobacillus arabinosus*, *Lactobacillus pentosus* and *Leuconostoc mesenteroides*.

¹² *Proc. Soc. Exp. Biol. Med.*, 1940, **43**, 151. ¹³ *J. Biol. Chem.*, 1941, **139**, 111.

¹⁴ *Ibid.*, 1941, **140**, 453. ¹⁵ *Ibid.*, p. 461. ¹⁶ *J. Bact.*, 1940, **36**, 273.

¹⁷ *J. Biol. Chem.*, 1941, **139**, 475. ¹⁸ *Proc. Nat. Acad. Sci.*, 1941, **27**, 1.

In concluding this section, reference may be made to an excellent review of growth-promoting nutritives for yeasts by R. J. Williams.¹⁹

Enzymes.—Papain. Following the preparation of crystalline papain by A. K. Balls and H. Lineweaver,²⁰ a further communication by A. K. Balls and E. F. Jensen²¹ describes the preparation of a new crystalline enzyme, which the authors propose to term chymopapain, by analogy with the chymotrypsin of M. Kunitz and J. H. Northrop.²² The new enzyme is extremely stable at 10° and p_H 2.0, and this fact was utilised in its preparation. At p_H 2.0 an extensive precipitation of protein from a suspension of coagulated papaya latex is effected by hydrochloric acid, and the protein remaining in solution is proteolytically active, but an inert fraction is still present. This is precipitated by half saturation with sodium chloride at p_H 4.0, and the active crystallisable material may be precipitated by addition of hydrochloric acid to the solution fully saturated with sodium chloride. The crystals obtained were much more soluble than the original papain under the same conditions, showed a strong positive nitroprusside reaction, and the amount present in latex was much greater than that of papain.

In further studies of the action of papain on proteins, H. Lineweaver and S. R. Hoover²³ find additional support for the suggestion that enzyme action is greater on denatured proteins than on the native protein. Thus, in the case of papain, it was found that the initial rate of digestion of hæmoglobin in the presence of at least six molar concentrations of urea is very much greater than in water solution only. The increase in digestibility is similar to, but not exactly parallel to, the decrease in solubility of hæmoglobin when denatured by urea. The increase in rate of hydrolysis of proteins when denatured appears to be comparable to the increase in reactivity of $-SH$, $-S-S-$ and tyrosine phenol groups. The method whereby denaturation is effected seems to have little effect on the rate of digestion. The increase in rate of digestion of a denatured protein is different for each enzyme, and that for a number of different proteins treated by a single enzyme is also different.

The widely adopted oxidation-reduction theory of papain activation is not in harmony with experimental facts observed by J. S. Fruton and M. Bergmann,²⁴ and, in a later paper, by these authors and G. W. Irving, jun.,²⁵ who do not accept this explanation. In the first instance, papain was activated by hydrocyanic acid, inactivated by precipitation with isopropyl alcohol, and the whole process repeated, at the end of which almost complete recovery of the original activity of the enzyme was observed. These facts are difficult of interpretation in terms of the disulphide-sulphydryl theory; moreover, the action of hydrocyanic acid on disulphide linkages will produce only one sulphydryl group: $R \cdot S \cdot SR' + HCN \longrightarrow R \cdot SH +$

¹⁹ *Biol. Rev.*, 1941, **16**, 49.

²¹ *J. Biol. Chem.*, 1941, **137**, 459.

²² *J. Biol. Chem.*, 1941, **137**, 325.

²³ *Ibid.*, 1941, **139**, 569.

²⁰ *Ann. Reports*, 1940, **37**, 429.

²² *J. Gen. Physiol.*, 1935, **18**, 433.

²⁴ *Ibid.*, 1940, **133**, 153.

R'-SCN. The authors suggest that a better explanation is afforded by supposing that hydrocyanic acid combines with papain to form a dissociable papain-hydrogen cyanide compound corresponding to the hydrogen cyanide activated enzyme. On precipitation with isopropyl alcohol, the compound dissociates and the precipitate consists of the hydrogen cyanide-free enzyme, inactive towards synthetic substrates. In the later paper it is pointed out that natural activators are usually present in preparations of proteinases, and minute quantities of these activators profoundly affect the response to added activators. In the case of papain it was found that, if the natural activators were removed by careful dialysis, subsequent addition of hydrocyanic acid involved no activation of the enzyme. The activation normally observed with hydrocyanic acid thus depends on the presence of natural activators, which may occur only in minute traces. Benzoyl-*L*-arginineamide being used as artificial substrate in the study of reaction kinetics, it has been found that the component of papain (and of beef spleen cathepsin) which hydrolyses the substrate may exist in two inactive forms. The α -form is not activated by hydrocyanic acid, but may be converted into the β -form, which is, and the activation consists in the formation of dissociable compounds of the activator and the β -form. It is noteworthy also that the activation does not involve the mutual transformation of disulphide and sulphydryl groups, nor is there any evidence of reduction or oxidation processes.

Urease.—The presence of sulphydryl groups in urease has been established, and the activation of the enzyme by certain reducing agents, and its inactivation by oxidising agents, suggest that the activity of the enzyme may be a function of oxidation-reduction potential. The activity of crystalline urease was determined by I. W. Sizer and A. A. Tytell,²⁶ who employed substrates which were adjusted at varying E_h by a number of oxidising and reducing agents used separately or in mixture, and also by the use of sodium sulphide and potassium permanganate at various concentrations. Curves similar to the familiar activity- p_H curves were obtained in all cases, and an optimum E_h of +150 mv. was indicated. The activity of crude urease, in contrast to that of crystalline urease, was unaffected by variations in E_h of the substrate. In a note to the paper it is pointed out that the E_h of the jack bean after soaking in water is +190 mv., a value in such close agreement with the optimum E_h of the enzyme as to suggest some physiological significance. The authors stress the somewhat empirical nature of their observations; but this is probably the first example of the production of activity- E_h curves, and examination of other enzymes in this aspect may yield important results.

An improved method for the preparation of crystalline urease is described by A. L. Dounce,²⁷ whose modification of the original method of J. B. Sumner²⁸ involves a very considerable shortening of the time required for crystallisation, thus avoiding denaturation of the enzyme.

²⁶ *J. Biol. Chem.*, 1941, **138**, 631.

²⁷ *Ibid.*, 1941, **140**, 307.

²⁸ *Ibid.*, 1926, **70**, 97.

Ribonuclease.—Crystalline ribonuclease isolated from fresh ox pancreas digests yeast nucleic acid, the products being of low molecular weight. M. Kunitz²⁹ describes the isolation and properties of the crystalline enzyme, which appears to be a protein of the albumin type of molecular weight about 15,000. The enzyme is stable over a wide range of p_H and particularly over the range p_H 2.0—4.5. Denaturation of the protein comprising the enzyme involves a corresponding loss in its activity. Similar values for the molecular weight have been found by A. Rothen,³⁰ who gives 12,700 from rate of sedimentation and diffusion data, and 13,000 from equilibrium measurements. The purified crystalline enzyme had an isoelectric point at p_H 7.8 by electrophoresis. All these values are in good agreement with those computed by I. Fankuchen,³¹ who has made crystallographic and X-ray studies of the enzyme and calculates 15,700 and 13,700 for the hydrated and the anhydrous protein respectively.

F. W. Allen and J. J. Eiler³² also have prepared the crystalline ribonuclease and have employed it in studies of its action on ribonucleic acid. It is possible that the enzyme is in the nature of a depolymerase, but available evidence points to the probability of a low degree, if any, of polymersation in the case of ribonucleic acid, although deoxyribonucleic acid probably exists in a highly polymerised state. K. Makino³³ and J. M. Gulland³⁴ hold that ribonucleic acid shows four primary phosphoric acid dissociable groups and no secondary phosphoric acid dissociations, and titration experiments by the above authors confirm this. The liberation of a fifth acidic group by the crystalline enzyme is thought to denote the opening of a cyclic structure such as that envisaged by H. Takahashi.³⁵

Proteins.—*Leaf proteins.* The preparation of the proteins of green leaves has involved a number of technical difficulties, and, since the preparation of spinach proteins by T. B. Osborne and A. J. Wakeman³⁶ in 1920, the investigations in this field have been carried out largely by A. C. Chibnall and his school. This work is so well known that a reference to his important book³⁷ must suffice here. Amongst recent publications on the subject, those of J. W. H. Lugg may be mentioned. In an early paper³⁸ he deals with the estimation of tyrosine and tryptophan in the hydrolysates of leaf proteins and suggests means of overcoming previous difficulties involving unsatisfactory results. This was followed³⁹ by a series of experiments whose main object was to determine the most satisfactory hydrolysis procedures with a view to subsequent estimation of tyrosine and tryptophan in the hydrolysates. Hydrolysis in sealed tubes at 100° with alkali or alkali stannite solutions was found to be satisfactory. Two further papers appeared in 1938⁴⁰ devoted to the partial analysis of protein preparations from grasses,

²⁹ *J. Gen. Physiol.*, 1940, **24**, 15.

³¹ *Ibid.*, p. 315.

³³ *Z. physiol. Chem.*, 1935, **236**, 201.

³⁵ *J. Biochem. Japan*, 1932, **16**, 463.

³⁷ "Protein Metabolism in the Plant," Yale Univ. Press, 1939.

³⁸ *Biochem. J.*, 1937, **31**, 1422.

⁴⁰ *Ibid.*, pp. 2114, 2123.

³⁰ *Ibid.*, p. 203.

³² *J. Biol. Chem.*, 1941, **137**, 757.

³⁴ *J.*, 1938, 1722.

³⁶ *J. Biol. Chem.*, 1920, **42**, 1.

³⁹ *Ibid.*, 1938, **32**, 775.

including cocksfoot and lucerne. The proteins were prepared by methods largely elaborated by A. C. Chibnall⁴¹⁻⁴³ and co-workers, and in the first instance the sulphur distribution was determined, it being shown that the contents of cystine and methionine were sufficiently high to conform to normal standards of the nutritional requirements of animals. Secondly, in addition to the sulphur distribution, the amide, tyrosine and tryptophan contents of leaf proteins of various *Gramineæ*, *Leguminosæ* and *Chenopodiaceæ* were determined. Here again it was shown that in respect of the above amino-acids, the leaf proteins compared favourably with other proteins of the animal diet. Later,⁴⁴ various methods of extraction of leaf proteins were employed, and the samples examined for representativeness. Addition of lipid solvents to mildly alkaline leaf juices allows most of the granule protein to pass into solution, whereas difficulty in avoiding loss of this fraction had previously been experienced. It was also shown that the presence of alcohol in the protein solutions near their isoelectric point rendered flocculation by acid, and coagulation by heat, more complete. In the latest paper to date, J. W. H. Lugg⁴⁵ finds that the amide, tryptophan and tyrosine contents of proteins of the photosynthesising tissues of some cryptogams are of the same order of magnitude as those of the leaf proteins of angiosperms of the spermatophyte division; the tryptophan content of preparations from *Pteridium aquilinum* is lower than any previously encountered.

The basic amino-acids of leaf proteins have been determined by G. R. Tristram,⁴⁶ who made a critical examination of methods available, and studied the influence of the presence of carbohydrates on the results obtained. More satisfactory estimation of the three bases in leaf proteins containing 12—16% of nitrogen was secured, but where the material was poor in protein, containing less than 8% of protein nitrogen, lysine only could be estimated reliably. As in the case of the amino-acids determined by J. W. H. Lugg (*v.s.*), there appears to be very little variation in content from species to species, nor is there much seasonal variation within a single species.

A. M. Smith and T. Wang⁴⁷ also have prepared proteins from grasses and have determined the sulphur distribution in proteins from four species. The amounts of cystine and methionine were substantially the same in all species; but it was observed that in proteins from samples that had reached or passed the flowering stage the amounts present were significantly higher than in those from young grass, or grass kept short by grazing.

General.—Knowledge of the proteins of the latex of *Hevea brasiliensis* is somewhat scanty, although there are strong indications of their importance in the complicated bio- and physico-chemical mechanism of rubber latex coagulation. Thus, it has been shown by C. Bondy and H. Freundlich⁴⁸ and by A. R. Kemp and W. G. Straitiff⁴⁹ that the stability of latex is

⁴¹ *Biochem. J.*, 1921, **15**, 60; 1922, **16**, 334.

⁴² *J. Biol. Chem.*, 1923, **55**, 333; 1924, **61**, 303.

⁴³ *Biochem. J.*, 1926, **20**, 108; 1933, **27**, 1879.

⁴⁴ *Ibid.*, 1939, **33**, 110.

⁴⁵ *Ibid.*, 1939, **33**, 1271.

⁴⁶ *Compt. rend. Lab. Carlsberg*, 1938, **22**, 89.

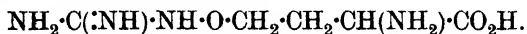
⁴⁵ *Ibid.*, 1940, **34**, 1549.

⁴⁷ *Ibid.*, 1941, **35**, 404.

⁴⁹ *J. Physical Chem.*, 1940, **44**, 78.

dependent upon the proteins present, and the coagulation point of the latex corresponds to their isoelectric point. G. R. Tristram⁵⁰ has isolated a protein from dried latex films and this product has a composition similar in many respects to that of the leaf proteins. The similarity is particularly marked in the case of the diamino- and dicarboxylic acids, and suggests a possible relationship, which is under investigation, between the proteins of the latex and of the leaves. In a further communication, G. R. Tristram⁵¹ gives analytical data for a protein prepared from crepe rubber. Close similarities between this and the latex protein suggest that there is only one protein in the latter, or that the product obtained from the latex is a mixture of several proteins. The main bulk of protein is undoubtedly precipitated from the latex and may be regarded as a representative fraction of the total protein. A loss of tryptophan in the crepe rubber protein is attributed to changes undergone in manufacture. G. S. Whitby and H. Greenberg⁵² provide a summary of the amino-acid composition of latex and latex proteins as published to date by previous workers. They have investigated the amino-acids present in the latex of *Hevea brasiliensis* and have isolated tyrosine, *l*-leucine, *d*-isoleucine, *d*-valine, *d*-arginine, *l*-aspartic acid and *i*-proline. Phenylalanine is also present but was not isolated.

The occurrence of the amino-acid citrulline, discovered by M. Wada⁵³ in the juice of the water melon (*Citrullus vulgaris*), has suggested to P. S. Krishnan and T. K. Krishnaswamy⁵⁴ the possibility that the seeds of the fruit may be a source of the amino-acid. The proteins and other nitrogenous substances of the seeds were investigated and a crystalline globulin was prepared. This represented the bulk of the protein, but a glutelin was also obtained in pure condition. Both proteins were analysed and both citrulline and canavanine, free or combined, were absent. Canavanine was originally isolated from jack bean by M. Kitagawa and T. Tomita⁵⁵ in 1929, and from soya bean meal by M. Kitagawa and S. Monobe⁵⁶ in 1933. It has been shown^{57, 58} to have the formula



A modified method of preparation is proposed by M. Damodoran and K. G. A. Narayanan⁵⁹ whereby increased yields of the amino-acid may be obtained from the seeds of *Canavalia obtusifolia*.

Reference has already been made to recent modifications in the methods of hydrolysis of proteins, and of the isolation and estimation of the products. In the space remaining, brief reference only may be made to further developments in protein analysis. For example, B. W. Town⁶⁰ publishes, in continuation of his studies^{61, 62} on the separation of amino-acids by means

⁵⁰ *Biochem. J.*, 1940, **34**, 301.

⁵¹ *Ibid.*, p. 640.

⁵² *Biochem. J.*, 1939, **33**, 1285.

⁵³ *J. Biochem. Japan*, 1933, **18**, 333.

⁵⁴ M. Kitagawa *et al.*, *J. Agric. Chem. Soc., Japan*, 1933, **9**, 845.

⁵⁵ J. M. Gulland and C. J. O. R. Morris, *J.*, 1935, 763.

⁵⁶ *Biochem. J.*, 1939, **33**, 1742.

⁵⁷ *Ibid.*, 1928, **22**, 1083.

⁵¹ *Ibid.*, 1941, **35**, 413.

⁵³ *Proc. Imp. Acad., Tokyo*, 1930, **6**, 15.

⁵⁵ *Proc. Imp. Acad., Tokyo*, 1929, **5**, 380.

⁶⁰ *Ibid.*, 1941, **35**, 417.

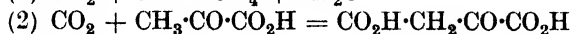
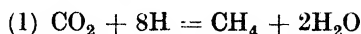
⁶² *Ibid.*, 1936, **30**, 1837.

of their copper salts, an investigation of the dicarboxylic acids of gliadin. He reports the isolation of *r*-glutamic acid, thought to be a true hydrolysis product and not an artefact. Some of the methods of hydrolysis and of estimation of the hydrolysis products adopted by J. W. H. Lugg (*v.s.*) have been utilised and found satisfactory by D. M. Doty,⁶³ who proposes more rapid methods for the estimation of some of the amino-acids, including tyrosine, tryptophan, arginine, histidine and cystine, in the grain of corn (maize). Amongst methods which have been applied almost solely to animal proteins, but which may be equally capable of application to plant proteins may be mentioned a micro-method for the determination of basic amino-acids based on a preliminary separation of these substances from the other hydrolysis products by electrical transport. A. A. Albanese,⁶⁴ the author of the method, follows this procedure by separation of arginine as flavianate with subsequent precipitation of the histidine as the mercuric chloride complex, and estimation of lysine from the residual nitrogen. Finally, M. Bergmann and his associates are developing a new principle whereby the components of a protein hydrolysate are determined by partial precipitation as salts, the amount remaining in solution being estimated from a known solubility product. Thus, M. Bergmann and W. H. Stein⁶⁵ estimate glycine by precipitation with potassium trioxalatochromate, and proline similarly with ammonium rhodanilate. The method has been adapted to a semimicro-scale by M. Bergmann and H. R. Ing,⁶⁶ the reaction products being filtered at the centrifuge. Glycine has been estimated in this case by means of sodium dioxypyridate, and proline as previously indicated.

F. W. N.

6. THE UTILISATION OF CARBON DIOXIDE BY HETEROTROPHIC BACTERIA AND ANIMAL TISSUES.

Carbon dioxide was for long regarded as a physiologically inert gas except in the case of photosynthetic and chemosynthetic organisms. The first suggestion to the contrary was the discovery that carbon dioxide facilitated the cultivation of the organism of contagious abortion, *Brucella abortus*.¹ In 1935 it was found that a number of common bacteria failed to develop in media from which carbon dioxide was rigorously removed.² It is now known that this gas reacts chemically in various organisms. So far two reactions can be defined :



It is highly probable that other reactions occur.

⁶³ *Ind. Eng. Chem. (Anal.)*, 1941, **13**, 169.

⁶⁴ *J. Biol. Chem.*, 1940, **134**, 467.

⁶⁵ *Ibid.*, 1939, **128**, 217.

⁶⁶ *Ibid.*, 1939, **129**, 603.

¹ T. Smith, *J. Exp. Med.*, 1924, **40**, 219.

² G. P. Gladstone, P. Fildes, and G. M. Richardson, *Brit. J. Exp. Path.*, 1935, **16**, 335. For a review of the literature up to 1938, see Hes, *Ann. Ferment.*, 1938, **4**, 547.

Early work on reaction (1) is well summarised by H. A. Barker.³ The key observation was that of Söhngen,⁴ who showed that enrichment cultures from soil fermented a mixture of hydrogen and carbon dioxide to methane; this is to be regarded as a reduction of carbon dioxide by molecular hydrogen analogous to the reduction of sulphate and nitrate catalysed by hydrogenase on the one hand and by sulphatase and nitratase respectively on the other. This analogy was pointed out by van Niel (quoted by Barker³), who postulated that the production of methane known to occur anaerobically from a rich variety of substrates was really an oxidation of the substrate with carbon dioxide acting as the hydrogen acceptor. Recently Barker and his co-workers have demonstrated that in a number of cases this is indeed so; the difficulty of isolating methane bacteria has been largely overcome and each species isolated has been shown to effect the oxidation of certain groups of compounds by hydrogen transfer to carbon dioxide. It now seems probable that the reduction of carbon dioxide is the sole means by which methane is formed in fermentations. Thus *Methanobacterium Omelianski*, isolated by Barker,⁴ oxidises the following alcohols in the presence of carbon dioxide to their corresponding acids: ethanol, *n*-propanol, *n*-butanol, *sec*-butanol and *n*-pentanol; methanol and *tert*-butanol are not attacked; isopropanol and isobutanol are oxidised to acetone and methyl ethyl ketone respectively. The fermentation of ethanol in growth experiments on synthetic media with ethanol as sole source of carbon occurs closely in accordance with the equation $2C_2H_5\cdot OH + CO_2 = 2CH_3\cdot CO_2H + CH_4$, the slight deficit found in the substances on the right side of the equation being due to the fact that about 6% of the carbon of the ethanol and 1.5% of the carbon dioxide are used to form cell material.⁵

Where mixed enrichment cultures from mud are used for the oxidation of the alcohols by carbon dioxide a second reaction sets in whereby the acids formed are further oxidised. Two organisms carrying out this second oxidation have been isolated, *Methanococcus Mazei* and *Methanobacterium Söhngeni*; ⁴ both ferment acetic and butyric acids but none of the alcohols. The fermentation of acetic acid proceeds according to the equation $CH_3\cdot CO_2H + 2H_2O + CO_2 = 2CO_2 + CH_4 + 2H_2O$. Butyric acid appears to give rise first to acetic acid, which is then further oxidised as above. These experiments, carried out on *Mb. Omelianski* and *Methanosarcine methanica*, showed furthermore that cell material as well as methane is produced by reduction of carbon dioxide.⁶

The reduction of carbon dioxide to acetic acid has been described by K. T. Wieringa.⁷ This observer repeated Söhngen's synthesis of methane from hydrogen and carbon dioxide with crude cultures from mud. On pasteurising the culture and plating out, he obtained a spore-forming organism by means of which carbon dioxide was reduced by hydrogen, giving no

³ *Arch. Mikrobiol.*, 1936, 1, 7, 404.

⁴ H. A. Barker, *ibid.*, 1936, ii, 7, 420.

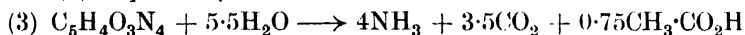
⁵ *Idem*, *J. Biol. Chem.*, 1941, 137, 153.

⁶ H. A. Barker, S. Ruben, and M. D. Kamen, *Proc. Nat. Acad. Sci.*, 1940, 26, 426.

⁷ *Antonie van Leeuwenhoek*, 1936, 3, 263.

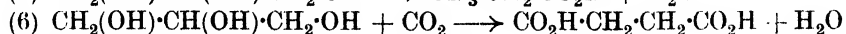
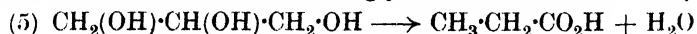
methane but a quantitative yield of acetic acid. There is no reason, however, to postulate acetic acid as an invariable intermediate in the Söhngen reaction, since there is a case on record in which the reaction has been effected by a culture derived from a single cell which was incapable of producing methane from any compound with more than one carbon atom.⁸

A special case of carbon dioxide reduction is that due to *Cl. acidii urici*.⁹ This organism decomposes uric acid, xanthine, hypoxanthine and guanine anaerobically, giving only ammonia, carbon dioxide, and acetic acid; purine, urea, allantoin, uracil and caffeine are unattacked; adenine, adenosine, guanosine and yeast nucleic acid are attacked slowly. Uric acid and hypoxanthine are decomposed closely in accordance with equations (3) and (4) respectively:



The fact that in (4) more than 1 mole of acetic acid was produced from 1 mole of hypoxanthine led to the hypothesis that the decomposition was due to an oxidoreduction with carbon dioxide, which is itself reduced to acetic acid as in the reaction reported by Wieringa. This was supported by experiments in which suspensions of the organism fermented uric acid in the presence of radioactive $^{11}\text{CO}_2$.¹⁰ The results showed that the acetic acid produced was radioactive and that the ^{11}C was present in the methyl as well as in the carbonyl group; also that ^{11}C had passed into cell material. So far the evidence supports the reduction of carbon dioxide to acetic acid. On the other hand, in experiments in which uric acid was fermented in a rapid stream of hydrogen free from carbon dioxide the rate of breakdown was the same as in the control; this evidence is against carbon dioxide acting as the hydrogen acceptor unless its concentration within the cell is sufficient to maintain the optimum rate in spite of its rapid removal from the solution.

A second line of investigation relating to carbon dioxide utilisation originated from work on the fermentation of propionic acid bacteria. In 1936 H. G. Wood and C. H. Werkman,¹¹ studying the fermentation of glycerol by these organisms, made the unexpected observation that the end-products of the fermentation—mainly propionic and succinic acids—contained more carbon than the fermented glycerol. A closer investigation showed that the additional carbon was derived from calcium carbonate which had been added to the medium, as is customary, to neutralise acids formed during the fermentation. In 1938 Wood and Werkman¹² showed that the quantities of succinic acid formed and carbon dioxide (or carbonate ion) used were approximately equimolecular. The experimental data conform with the assumption that there are two main reactions when glycerol is fermented, namely,



⁸ M. Stephenson and L. H. Stickland, *Biochem. J.*, 1933, **27**, 1617.

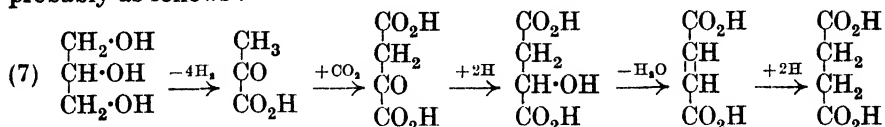
⁹ H. A. Barker and J. V. Beck, *J. Biol. Chem.*, 1941, **41**, 3.

¹⁰ H. A. Barker, S. Ruben, and J. V. Beck, *Proc. Nat. Acad. Sci.*, 1940, **26**, 477.

¹¹ *Biochem. J.*, 1936, **30**, 48.

¹² *Ibid.*, 1938, **32**, 1262.

Later work ^{13, 14} has shown that the intermediate stages of reaction (6) are probably as follows :



This scheme is supported by the facts that the carbon dioxide used and the succinic acid formed are equimolecular; ¹² that the utilised carbon dioxide is present in the carboxyl group of succinic acid ¹³ (as shown by experiments with ¹³C); that fumaric and malic acids are formed along with succinic acid; ¹⁴ that the reactions postulated readily occur.¹⁵

Many micro-organisms form succinic acid when fermenting carbohydrates, glycerol, or pyruvic acid. It is likely that in most cases succinic acid is formed according to reactions (2) and (7). That this is true for *Bact. coli* has been shown with the help of carbon isotopes.^{13, 14}

Reaction (2) probably plays a rôle in the synthesis of citric acid, fumaric acid and related substances in moulds.^{16, 17}

That carbon dioxide can be utilised in animal tissues by combining with pyruvic acid [reaction (2)] was first suggested by H. A. Krebs and L. V. Eggleston,¹⁸ who showed that in pigeon liver pyruvic acid yields the same products as oxaloacetic acid,¹⁹ viz., citric acid, α -ketoglutaric acid, succinic acid, fumaric acid and malic acid. The obvious, and in fact only satisfactory, explanation was the assumption that pyruvic acid is first converted into oxaloacetic acid, by way of reaction (2); this hypothesis was supported by the fact that the concentration of carbon dioxide determined the rate of conversion of pyruvic acid into the above-named products. Final proof for the occurrence of reaction (2) in pigeon liver was supplied by E. A. Evans, jun., and L. Slotin,²⁰ who added bicarbonate containing ¹¹C and found α -ketoglutaric acid to contain the isotope. This was confirmed by Wood *et al.*,¹³ who used the isotope ¹³C. These authors determined the position of the fixed carbon dioxide and found that all the fixed carbon was in the carboxyl group next to the ketone group. This indicates that citric acid is not an intermediate in the formation of α -ketoglutaric acid, for if the latter acid was derived from a symmetrical molecule the fixed carbon should be equally distributed in the two carboxyl groups. The authors suggest the following

¹³ H. G. Wood, C. H. Werkman, A. Hemingway, and A. D. Nier, *J. Biol. Chem.*, 1940, **135**, 781; 1941, **139**, 365, 377; S. F. Carson and S. Ruben, *Proc. Nat. Acad. Sci.*, 1940, **26**, 422; S. F. Carson, J. W. Foster, S. Ruben, and H. A. Barker, *ibid.*, 1941, **27**, 229.

¹⁴ H. A. Krebs and L. V. Eggleston, *Biochem. J.*, 1941, **35**, 676.

¹⁵ H. A. Krebs, *Nature*, 1941, **147**, 560.

¹⁶ Y. Nishina, S. Endo, and H. Nakayama, *Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1941, **38**, 341.

¹⁷ H. G. Wood and C. H. Werkman, *Biochem. J.*, 1940, **34**, 7.

¹⁸ *Ibid.*, p. 1383.

¹⁹ See *Ann. Reports*, 1937, **34**, 418.

²⁰ *J. Biol. Chem.*, 1940, **136**, 301; 1941, **141**, 439.

scheme for the formation of α -ketoglutaric acid : pyruvic acid + oxaloacetic acid \longrightarrow *cis*-aconitic acid $\xrightarrow{+H_2O}$ isocitric acid $\xrightarrow{-2H}$ α -ketoglutaric acid + CO_2 .

Solomon *et al.*²¹ injected $NaH^{11}CO_3$ and lactate into fasting rats and found the liver glycogen to contain ^{11}C . This can be explained on the assumption that the primary reaction is again reaction (2).

Prior to this work S. Ruben and M. D. Kamen²² had already shown with the help of isotopes that liver incorporates carbon dioxide or bicarbonate into organic compounds. These authors, however, did not define the compounds containing the isotope; it may have been urea, which has long been supposed to be formed from carbon dioxide and ammonia;²³ E. A. Evans and L. Slotin, using $^{11}CO_2$, have recently supplied final proof for the correctness of this assumption.²⁴

M. S.
H. A. K.

7. METABOLIC PRODUCTS OF THE LOWER FUNGI.

In the short space available it is not possible to review adequately progress in this field since it was last dealt with in these *Annual Reports*. Interested readers are therefore referred to *Annual Review of Biochemistry*, 1940, 9, 571, for a detailed account to the end of 1939. Attention will be confined here to work published subsequently.

(a) *Derivatives of Toluquinone*.—Fumigatin was first described as a metabolic product of *Aspergillus fumigatus* Fresenius by W. K. Anslow and H. Raistrick.¹ The molecular constitution, 3-hydroxy-4-methoxy-2:5-toluquinone, ascribed to it by these authors has been confirmed by synthesis.²

(b) *Derivatives of 2-Methylantraquinone*.—Catenarin, present in the mycelium of different species of *Helminthosporium*, particularly *Helminthosporium catenarium* Drechsler,³ has now been shown to be 1:4:5:7-tetrahydroxy-2-methylantraquinone.⁴ This conclusion was confirmed by synthesis.⁵ Erythroglaucin, from species in the *Aspergillus glaucus* series,⁶ has been shown by Anslow and Raistrick⁷ to be 1:4:5-trihydroxy-7-methoxy-2-methylantraquinone and was prepared by them *in vitro* by methylating catenarin with methyl iodide and sodium methoxide in methanol solution. Cynodontin, 1:4:5:8-tetrahydroxy-2-methylantraquinone,

²¹ A. K. Solomon, B. Vennesland, F. W. Klemperer, J. M. Buchanan, and A. B. Hastings, *J. Biol. Chem.*, 1941, **140**, 171.

²² *Proc. Nat. Acad. Sci.*, 1940, **27**, 418.

²³ H. A. Krebs and K. Henseleit, *Z. physiol. Chem.*, 1932, **210**, 33.

²⁴ *J. Biol. Chem.*, 1940, **136**, 806. ¹ *Biochem. J.*, 1938, **32**, 687.

² W. Baker and H. Raistrick, *J.*, 1941, 670.

³ J. H. V. Charles, H. Raistrick, (Sir) R. Robinson, and A. R. Todd, *Biochem. J.*, 1933, **27**, 499; H. Raistrick, (Sir) R. Robinson, and A. R. Todd, *ibid.*, 1934, **28**, 559.

⁴ W. K. Anslow and H. Raistrick, *ibid.*, 1940, **34**, 1124.

⁵ *Idem*, *ibid.*, 1941, **35**, 1006.

⁶ J. N. Ashley, H. Raistrick, and T. Richards, *ibid.*, 1939, **33**, 1291.

⁷ *Ibid.*, 1940, **34**, 1124.

from *Helminthosporium cynodontis* Marignoni,⁸ has also been synthesised by Anslow and Raistrick.⁹

H. G. Hind¹⁰ isolated from cultures of *Penicillium carmino-violaceum* Biourge two polyhydroxyanthraquinones, carviolacin, $C_{20}H_{16}O_7$, and carviolin, $C_{16}H_{12}O_6$, and later¹¹ showed that carviolin is a monomethyl ether of ω -hydroxyemodin, 4 : 5 : 7-trihydroxy-2-hydroxymethylanthraquinone, which was itself isolated from cultures of *Penicillium cyclopium* Westling by W. K. Anslow, J. Breen, and H. Raistrick¹² and from *Penicillium citreo-roseum* Dierckx by T. Posternak.¹³ Posternak¹⁴ showed that roseopurpurin, which he isolated from *Penicillium roseo-purpureum* Dierckx, is the 4-methyl ether of ω -hydroxyemodin, i.e., 5 : 7-dihydroxy-4-methoxy-2-hydroxymethylanthraquinone. The present reviewer (unpublished observation) has compared Hind's carviolin and Posternak's roseopurpurin, received from their respective discoverers, and has shown that they are one and the same substance.

Penicillipsin, $C_{30}H_{24}O_8$, the orange crystalline colouring matter of *Penicillopsis clavariaeformis* Solms-Laubach,¹⁵ when oxidised in air and subsequently irradiated, gives chocolate-brown needles of irradiated oxy-penicillipsin, $C_{30}H_{20}O_9$. This substance is closely related to, but not identical with, hypericin, the photodynamically active colouring matter of St. John's wort, *Hypericum perforatum*. Penicillipsin, whose constitution is at present unknown, is a derivative of 2-methylanthraquinone, since it gives tetranitroemodin on oxidation with nitric acid.

(c) *Chlorine-containing Metabolic Products*.—The conversion by moulds of inorganic chlorides in the culture medium, e.g., potassium chloride, into organic chlorine-containing metabolic products is becoming increasingly recognised. A survey of the subject was made by P. W. Clutterbuck, S. L. Mukhopadhyay, A. E. Oxford, and H. Raistrick,¹⁶ and these workers isolated from the metabolism solution of *Caldariomyces fumago* Woronichin crystalline caldariomyecin, $C_5H_8O_2Cl_2$, the most probable structure for which is 2 : 2-dichlorocyclopentane-1 : 3-diol. T. P. Curtin and J. Reilly¹⁷ isolated from the mycelium of *Penicillium sclerotiorum* van Beyma a yellow crystalline colouring matter, sclerotiorine, to which the improbable empirical formula $C_{20}H_{20}O_5Cl$ was assigned. Its molecular structure has not yet been determined.

(d) *Anti-bacterial Substances from Moulds*.—The fact that many mould metabolic products have marked bacteriostatic or even bactericidal properties is becoming increasingly evident. A. Fleming¹⁸ showed that culture

⁸ H. Raistrick, R. Robinson, and A. R. Todd, *Biochem. J.*, 1933, **27**, 1170.

⁹ *Ibid.*, 1940, **34**, 1546.

¹⁰ *Ibid.*, p. 67.

¹¹ *Ibid.*, p. 577.

¹² *Ibid.*, p. 159.

¹³ *Compt. rend. Soc. Phys. Hist. nat. Genève*, 1939, **56**, 28; T. Posternak and J. P. Jacob, *Helv. Chim. Acta*, 1940, **23**, 237.

¹⁴ *Helv. Chim. Acta*, 1940, **23**, 1046.

¹⁵ A. E. Oxford and H. Raistrick, *Biochem. J.*, 1940, **34**, 790.

¹⁶ *Ibid.*, p. 664.

¹⁷ *Ibid.*, p. 1419.

¹⁸ *Brit. J. Exp. Path.*, 1929, **10**, 226.

filtrates from a strain of *Penicillium notatum* Westling contain a substance, penicillin, which is highly bacteriostatic against Gram-positive micro-organisms. Optimum cultural conditions for the formation of penicillin and the fact that it is extractable with ether were established by P. W. Clutterbuck, R. Lovell, and H. Raistrick.¹⁹ H. W. Florey *et al.*²⁰ have recorded striking successes in the use of penicillin concentrates in clinical trials and describe the preparation of an intensely active, but at present impure, barium salt of penicillin. Penicillin is relatively non-toxic to animals. E. C. White²¹ reports that culture filtrates from strains in the *Aspergillus flavus* series contain a bactericidal agent and G. A. Glister²² has shown that an unnamed species of *Aspergillus* produces a powerful anti-bacterial agent which is particularly active against Gram-negative organisms. Neither of these substances has at present been isolated in a pure condition. S. A. Waksman and H. B. Woodruff²³ have isolated from soil a new species, *Actinomyces antibioticus*,²⁴ which produces two crystalline substances, actinomycin A and actinomycin B. Actinomycin A is intensely bacteriostatic against Gram-positive bacteria, but only moderately so against Gram-negative bacteria. It is extremely toxic to animals.²⁵ Actinomycin B has little bacteriostatic action but is strongly bactericidal. Citrinin, $C_{13}H_{14}O_5$, a semi-quinonoid crystalline metabolic product of *Penicillium citrinum* Thom,²⁶ and penicillic acid, the β -methyl ether of γ -hydroxy- γ -isopropylidene-tetronic acid, a crystalline metabolic product of *Penicillium cyclopium* Westling,²⁷ have been shown to be powerful anti-bacterial agents.²⁸ Their activity against a wide range of micro-organisms has been determined by A. E. Oxford.²⁹ None of the above-mentioned substances, except possibly actinomycin A, is as active as penicillin against Gram-positive organisms, though Glister's substance, penicillic acid, and citrinin are much more active than penicillin against Gram-negative organisms.

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A. NEUBERGER.

F. W. NORRIS.

H. RAISTRICK.

M. STEPHENSON.

¹⁹ *Biochem. J.*, 1932, **26**, 1907.

²⁰ *Lancet*, 1940, **239**, 226; 1941, **241**, 177.

²¹ *Science*, 1940, **92**, 127.

²² *Nature*, 1941, **148**, 470.

²³ *Proc. Soc. Exp. Biol. Med.*, 1940, **45**, 609. ²⁴ *Idem*, *J. Bact.*, 1941, **42**, 231.

²⁵ S. A. Waksman, H. Robinson, H. J. Metzger, and H. B. Woodruff, *Proc. Soc. Exp. Biol. Med.*, 1941, **47**, 261.

²⁶ A. C. Hetherington and H. Raistrick, *Phil. Trans.*, 1931, **B**, **220**, 269; F. P. Coyne, H. Raistrick, and (Sir) R. Robinson, *ibid.*, p. 297.

²⁷ J. H. Birkinshaw, A. E. Oxford, and H. Raistrick, *Biochem. J.*, 1936, **30**, 394.

²⁸ H. Raistrick and G. Smith, *Chem. and Ind.*, 1941, **60**, 828; A. E. Oxford, H. Raistrick, and G. Smith, *ibid.*, 1942, **61**, 22.

²⁹ *Ibid.*, 1942, **61**, 48.

ANALYTICAL CHEMISTRY.

1. INTRODUCTION.

ALTHOUGH the scope and utility of the newer physical methods of analysis reported in the past three years cover the whole field of Chemistry, nevertheless reference to much of the progress in inorganic and organic analysis has of necessity been hitherto omitted, an omission which in this Report is in part remedied.

It is usually comparatively simple to detect and determine a substance when it is not accompanied by chemically related entities, but the analyst is frequently confronted with the problem of determining one or more constituents of a mixture of substances having similar characteristics. The alkali metals form a well-known group presenting such difficulties, and a section of this Report records recent progress and the application of the Lundegårdh and the Ramage technique which depend on the volatility and light-emitting properties of these elements in flames. Organic analysis has many problems presented by mixtures, and amongst them is the analysis of essential oils which has not so far been considered in these Reports. In view of the extensive and widening range of application of these oils in perfumery, medicine, etc., in recent years, the subject seems of sufficient importance to be considered here.

The use, in commerce, of the simpler oxygen-containing organic compounds has expanded considerably within recent years. This is doubtless due to the more ready availability of such materials on account of their increased production by methods, often novel, that have now been introduced into large-scale manufacture, while the substitution of compounds, *e.g.*, isopropyl alcohol in place of ethyl alcohol, that is thus rendered possible frequently relieves the material of legal restriction. Since the last report on alcohols (*Ann. Reports*, 1933, 30, 275) many new methods of analysis, as well as modifications of existing methods, have been proposed for detecting and estimating these compounds, with increased accuracy, in materials that often vary enormously in type and complexity. In this Report, some salient features of these advances are recorded.

The significance of trace substances in metabolism is receiving increasing recognition, and in spite of the general decline in the volume of work published during the past year, vitamins have not suffered from lack of interest. The importance of carbohydrates in industry and in metabolism needs no emphasis, and the papers which have appeared since the Report of 1938 justify further sections on the analysis of carbohydrates and of vitamins.

2. VITAMINS.

Much of the published work relates to improved processes for extracting the vitamins for analysis from natural products and to modifications of methods

of determination already reported,¹ but limitations of space permit reference to only a proportion of the papers which illustrate, rather than include all of, the progress which has been made.

Vitamin-A.—Discrepancies between biological, chemical, and spectrophotometric determinations of vitamin-A continue to be investigated.² Physicochemical determination of vitamin-A in fish-liver oils leads to a lower value than biological assay owing to the presence of esterified vitamin-A which is more stable than the free alcohol.³ The esterified vitamin appears to be more potent than the non-esterified,⁴ and some results lead to the view that the esters vary in activity among themselves.⁵ Investigations with the crystalline vitamin and its esters⁶ may be expected to throw light on the origin of the discrepancies.

The necessity for precaution against loss of vitamin as a result of oxidation during extraction for determination is well known, but significant loss by photodecomposition may also occur unless ultra-violet light is excluded, for example, by using amber-glass apparatus.⁷ When the unsaponifiable matter from cod-liver oil is dissolved in isopropyl alcohol or dehydrated ethyl alcohol, the spectrophotometric results are about 12% higher than when cyclohexane is used,⁸ which emphasises the importance of the solvent.

Vitamin-B Factors.—Optimum conditions have been investigated for the extraction of vitamin-B₁ (thiamin, aneurin), the hydrolysis of the phosphorylated aneurin with enzyme preparations, adsorption of the total vitamin on zeolites whereby interfering substances are removed, elution, and the oxidation with sodium hydroxide and potassium ferricyanide to thiochrome, which is determined by fluorescence measurement.⁹ In the initial extraction with dilute sulphuric acid, riboflavin (a member of the vitamin-B₂ complex) accompanies the -B₁ and, after the enzymic hydrolysis, may be separated by passing the solution first through "Decalso" (a synthetic zeolite) which adsorbs the -B₁ and then through "Supersorb" fuller's earth which adsorbs the riboflavin. The vitamins are eluted, and determined by measurement of fluorescence.¹⁰

A microbiological method¹¹ for riboflavin, in which the growth response of bacteria is measured in terms either of culture turbidity after 24 hours' incubation or of acidity produced as a result of 72 hours' incubation, shows good selectivity and reproducibility, and other vitamins, even in large

¹ *Ann. Reports*, 1938, **35**, 399; 1940, **37**, 463, 465, 467.

² *E.g.*, J. B. Wilkie, *Ind. Eng. Chem. (Anal.)*, 1941, **13**, 209; N. H. Coy, H. L. Sassaman, and A. Black, *ibid.*, p. 74.

³ W. Grab and T. Moll, *Klin. Woch.*, 1939, **18**, 563.

⁴ T. Moll and A. Reid, *Z. physiol. Chem.*, 1939, **260**, 9.

⁵ G. Lunde and H. Kringstad, *Tids. Kjemi*, 1940, **20**, 14.

⁶ J. G. Baxter and C. D. Robeson, *Science*, 1940, **92**, 203.

⁷ N. D. Embree, *Ind. Eng. Chem. (Anal.)*, 1941, **13**, 144.

⁸ D. C. M. Adamson and N. Evers, *Analyst*, 1941, **66**, 106.

⁹ D. J. Hennessy and L. R. Cerecedo, *J. Amer. Chem. Soc.*, 1939, **61**, 179; R. T. Connor and G. J. Straub, *Ind. Eng. Chem. (Anal.)*, 1941, **13**, 380.

¹⁰ *Idem*, *ibid.*, p. 385.

¹¹ E. E. Snell and F. M. Strong, *ibid.*, 1939, **11**, 346.

excess, do not interfere.¹² Microbiological¹¹ and fluorescence¹³ methods are preferred to a colorimetric method.¹⁴

Vitamin-B₆ (*adermin*, *pyridoxin*) is extracted from dilute solution by means of butyl alcohol or on zeolite, and is determined by means of the blue colour produced by 2:6-dichlorobenzoquinonechloroimide and a solution containing not less than 0.05 mg.% of -B₆. Methods of eliminating many interfering substances are described.¹⁵ The colour reaction with diazotised sulphanilic acid is not specific for -B₆, but interfering substances can be removed, and results are in approximate accord with bio-assays.¹⁶ Chemical methods for nicotinic acid and -B₆ have been reviewed.¹⁷

The application of the polarograph¹⁸ to the detection and determination of trace substances is being investigated extensively, and it is found that vitamin-B₁, nicotinic acid (pellagra-preventive factor), pantothenic acid (chick-pellagra factor), vitamin-B₆, and, most easily, riboflavin are reduced at the dropping-mercury electrode and give characteristic polarographic waves by which it is suggested that these substances, especially riboflavin, may be determined in natural products.¹⁹

Vitamin-D.—The sensitivity of the pink colour reaction (absorption max. at 5000 Å.) with antimony trichloride is increased by the presence of 2% of acetyl chloride, thereby permitting 2 µg. of vitamins-D₂ and/or -D₃ to be determined.²⁰ Fair agreement with bio-assays has been obtained when the antimony trichloride reaction is applied either to fish-liver oils containing more than 10,000 I.U. per g. and corrections are applied for the presence of sterols and vitamin-A, or to the non-saponifiable fraction which has been treated with maleic anhydride to destroy vitamin-A, carotenoids, and 7-dehydrocholesterol.²¹

Of several colour reactions investigated,²² the most selective is said to be that of Tortelli and Jaffé in which a blue colour (absorption bands at 5450—5500 and 5900—6000 Å.) is produced by the action of a solution of bromine in chloroform, and since vitamin-A, carotene, and oxidation products and isomerides of vitamin-D do not interfere, the reaction permits the determination of vitamin-D in, e.g., 0.01—0.05 ml. of cod-liver oil.

Discrepancies between different determinations of the extinction coefficient of calciferol (vitamin-D₂) have been traced to decomposition by the

¹² A. D. Emmett, O. D. Bird, R. A. Brown, C. Peacock, and J. M. Vandenbelt, *Ind. Eng. Chem. (Anal.)*, 1941, **13**, 219.

¹³ A. Z. Hodson and L. C. Norris, *J. Biol. Chem.*, 1939, **131**, 621.

¹⁴ A. R. Kemmerer, *J. Assoc. Off. Agric. Chem.*, 1940, **23**, 346; 1941, **24**, 413.

¹⁵ J. V. Scudi, *J. Biol. Chem.*, 1941, **139**, 707.

¹⁶ M. Swaminathan, *Nature*, 1940, **145**, 780.

¹⁷ H. A. Waisman and C. A. Elvehjem, *Ind. Eng. Chem. (Anal.)*, 1941, **13**, 221.

¹⁸ Cf. *Ann. Reports*, 1938, **35**, 389.

¹⁹ J. J. Lingane and O. L. Davis, *J. Biol. Chem.*, 1941, **137**, 567.

²⁰ C. H. Nield, W. C. Russell, and A. Zimmerli, *ibid.*, 1940, **136**, 73.

²¹ N. A. Milas, R. Heggie, and J. A. Reynolds, *Ind. Eng. Chem. (Anal.)*, 1941, **13**, 227.

²² V. L. Solianikova, *Biochimica*, 1939, **4**, 483.

light used in the determination, and a continuous-flow technique is recommended to eliminate the effect.²³

Vitamin-K.—Vitamin- K_2 (2-methyl-3-phytyl-1:4-naphthaquinone) is determined polarographically in solution of potassium chloride in aqueous isopropyl alcohol,²⁴ and $-K_1$ and related quinones are determined in 95% *n*-butyl alcohol by reduction and subsequent titration with 2:6-dichlorophenolindophenol. Vegetable and cod-liver oils and vitamins-A and -E cause no interference.²⁵

In a colorimetric method less than 0.1 mg. of 2-methyl-1:4-naphthaquinone or related compound in a drop of alcohol is treated with 2:4-dinitrophenylhydrazine and then successively with ammonia, amyl alcohol, and water, whereby a stable green colour, proportional to the quantity of the quinone, is extracted in the amyl alcohol.²⁶

3. ANALYSIS OF ALKALI METALS.

A. Chemical Methods.

The removal of all other metals, and all non-metals save chloride and occasionally sulphate ions, is the usual preliminary to the determination of the alkali metals. Recent editions of standard analytical works describe in detail accepted procedures of assembling the alkali metals. When only one member of the group is present it may be weighed as sulphate, but when, as is more usual, two or more members are together then it is customary to obtain a solution of their chlorides. Occasionally this may be easily achieved by dissolution in hydrochloric acid, but commonly this simple treatment fails, and one of the standard procedures of opening up the sample has to be employed. One such method, originally used by J. J. Berzelius, is the treatment of the sample with a mixture of hydrofluoric and sulphuric acids, followed by removal of all other metals and conversion of the sulphates into chlorides with barium chloride, the excess barium being removed by treatment with ammonium hydroxide and carbonate. Alternatively, the method of J. Lawrence Smith may be used, in which the sample is decomposed by heating with a mixture of ammonium chloride and calcium carbonate; the water extract contains the alkali chlorides, sulphates, and considerable amounts of calcium. This classical method has the advantage of leaving in the insoluble residue the bulk of any boron present in the sample, and all but a trace of magnesium. Most of the extracted calcium is removed by ammonium hydroxide and carbonate, and traces by ammonium oxalate.

Modifications of the Lawrence Smith method have recently been reported. W. van Tongeren¹ first prepares a liquid by treating 0.5 g. of calcium

²³ S. K. Crews and E. L. Smith, *Analyst*, 1939, **64**, 568.

²⁴ E. B. Hershberg, J. K. Wolfe, and L. F. Fieser, *J. Amer. Chem. Soc.*, 1940 **62**, 3516.

²⁵ N. R. Trenner and F. A. Bacher, *J. Biol. Chem.*, 1941, **137**, 745.

²⁶ A. Novelli, *Science*, 1941, **93**, 358.

¹ *Zentr. Min.*, 1936, A., 243; *Chem. Zentr.*, 1936, ii, 3929.

carbonate with an amount of concentrated hydrochloric acid just insufficient to cause complete dissolution. Under this liquid the sample is powdered, and additional calcium carbonate is added, together with a little ethyl alcohol. After drying and fusion, the cooled melt disintegrates in hot water. The use of barium chloride as a flux in place of the ammonium chloride has also been recommended: ² the preliminary slow heating to remove ammonia is thereby eliminated, and sulphates are automatically removed. Recent comparison of the Berzelius with the Lawrence Smith method and its modifications has been made.³ The possibility of boric, lead, or bismuth oxides being used as the decomposing agent has long been known; E. Schulek and L. Szlatinay ⁴ have recommended the use of boric acid in the analysis of organic compounds and mixtures containing alkali metal, halogen, sulphur, and arsenic. The addition of glucose ensured the reduction of arsenates and sulphates. J. Haslam and J. Beeley ⁵ have determined sodium and potassium in refractory materials by means of a modification of the Lawrence Smith method, the potassium being finally determined as perchlorate, and the sodium by zinc uranyl acetate.

The alkali metals having been separated from the other groups, their identification and determination present problems which continue to receive attention. Confirmatory drop tests for lithium, sodium, potassium, and caesium have been described.⁶ O. G. Scheintzis ⁷ finds that characteristic microcrystals form when a drop of borofluoric acid is added to a drop of solution containing amounts of potassium, rubidium, or caesium of the order of 1 µg.; some thirty elements and radicals were found not to interfere. Nickelous ions, in the presence of disodium hydrogen phosphate, have been observed ⁸ to give characteristic crystals of NiCsPO_4 and NiRbPO_4 with caesium and rubidium respectively. The test may be used for the detection of as little as 0.01% of caesium, or 0.1% of rubidium. Naphthol-yellow-S (the potassium salt of 2 : 4-dinitro- α -naphthol-7-sulphonic acid) gives a yellow precipitate with rubidium or potassium, but not with other alkali metals; this observation is made the basis of a microscopic detection method for as little as 6.8 µg. of rubidium.

There have been no recent developments in the *chloroplatinate* method, whereby potassium, rubidium, and caesium are precipitated by chloroplatinic acid from solutions of the alkali chlorides from which ammonium salts are absent. The cost of the reagent, and the fact that the composition of the precipitate may differ slightly from M_2PtCl_6 ($\text{M} = \text{K}, \text{Rb}, \text{or Cs}$), have combined in causing the *perchlorate* method to be preferred. Using the latter method, T. Kato ⁹ extracts the perchlorates of the alkali metals with methyl acetate. The residue consists of the potassium, rubidium, and

² R. E. Stevens, *Ind. Eng. Chem. (Anal.)*, 1940, **12**, 413.

³ E. Büttner, *Keram. Runds.*, 1939, **47**, 101.

⁴ *Z. anal. Chem.*, 1938, **112**, 336.

⁵ *Analyst*, 1941, **66**, 185.

⁶ J. I. Adams, A. A. Benedetti-Pichler, and J. T. Bryant, *Mikrochem.*, 1939, **26**, 29.

⁷ *J. Appl. Chem. Russia*, 1940, **13**, 1101.

⁸ M. V. Gapchenko, *ibid.*, p. 1264.

⁹ *J. Electrochem. Assoc. Japan*, 1935, **3**, 276.

cæsium salts which are separated by differences in the solubilities of their acid tartrates and phosphotungstates. Lithium and sodium are separated by the difference in solubility of their chlorides in aqueous ammonia. More usually, of course, the alkali chlorides are converted into perchlorates, and the sodium and lithium extracted with ethyl alcohol or with a mixture of *n*-butyl alcohol and ethyl acetate.¹⁰ From the latter solution the sodium may be precipitated as chloride by adding butyl alcohol saturated with hydrochloric acid gas, and the lithium in the filtrate converted into sulphate.

The use of zinc uranyl acetate¹¹ as a quantitative precipitant for sodium has been extensively developed. The precipitation of the complex $(\text{UO}_2)_3\text{ZnNa}(\text{CH}_3\text{CO}_2)_9 \cdot 6\text{H}_2\text{O}$ is satisfactorily obtained from the solution of the alkali chlorides; NH_4^+ , Mg^{++} , Ca^{++} , Ba^{++} , K^+ (if > 50 mg./ml.), do not interfere, but Li^+ , Sr^{++} , certain organic acids, phosphates, and sulphates in the presence of potassium, should be absent. R. Lindner and P. L. Kirk¹² report the use of this reagent for the determination of $0.13\text{--}4.13 \times 10^{-6}$ g. of sodium. The precipitate is redissolved in 5% sulphuric acid solution, reduced with metallic cadmium, and the uranium titrated with ceric sulphate. The method is applicable to biological materials. The sodium content of biological fluids (*e.g.*, serum, urine) has also been determined¹³ volumetrically (by titration of the triple salt with 0.1*N*-sodium hydroxide), and gravimetrically by means of modifications of the zinc uranyl acetate method. The use of this reagent in the gravimetric determination of sodium in natural waters has been described.¹⁴ The conditions for the precipitation of sodium by magnesium uranyl acetate have also been investigated by E. C. Elliott,¹⁵ with particular reference to the possibility of interference by certain elements. The moisture content of $\text{NaMg}(\text{or Zn})(\text{UO}_2)_3(\text{CH}_3\text{CO}_2)_9$ has been found to be 6–6.8% according to the humidity of the air.¹⁶ Certain uranyl acetate reagents for sodium also precipitate lithium from concentrated solutions, but copper uranyl acetate¹⁷ appears to be nearly specific for sodium, to which it is moderately sensitive.

Methods for lithium include its determination as stearate;¹⁸ phosphate;¹⁹ arsenate;²⁰ and the triple acetate,²¹ $\text{LiZn}(\text{UO}_2)_3(\text{CH}_3\text{CO}_2)_9 \cdot 6\text{H}_2\text{O}$, after extraction of the lithium by amyl alcohol and acetone. Many methods are based on the differential solubility of lithium chloride, and a number of solvents have served this purpose: ethyl alcohol,²² a mixture of butyl alcohol

¹⁰ Numerous workers, including H. H. Willard and G. F. Smith, *J. Amer. Chem. Soc.*, 1922, **44**, 2816; G. F. Smith and J. R. Ross, *ibid.*, 1925, **47**, 774, 1020.

¹¹ H. H. Barber and I. M. Kolthoff, *ibid.*, 1928, **50**, 1629.

¹² *Mikrochem.*, 1938, **23**, 269.

¹³ M. Dreguss, *Biochem. Z.*, 1939, **303**, 69.

¹⁴ O. Oparina, *Hydrochem. Mat.*, 1939, **11**, 96.

¹⁵ *Ind. Eng. Chem. (Anal.)*, 1940, **12**, 416.

¹⁶ N. Schoorl, *Chem. Weekblad*, 1939, **36**, 122.

¹⁷ E. R. Caley and W. O. Baker, *Ind. Eng. Chem. (Anal.)*, 1939, **11**, 604.

¹⁸ E. R. Caley, *J. Amer. Chem. Soc.*, 1930, **52**, 2754.

¹⁹ B. Brauner, *Coll. Czech. Chem. Comm.*, 1930, **2**, 442.

²⁰ T. Gaspar, *Anal. Fis. Quím.*, 1932, **30**, 406.

²¹ C. C. Miller and F. Traves, *J.*, 1936, 1395.

²² S. Palkin, *J. Amer. Chem. Soc.*, 1916, **38**, 2326.

and ethyl acetate,¹⁰ amyl alcohol and pyridine,²³ acetone.²⁴ A sensitive test for lithium, the sensitivity of which is so increased by the presence of sodium that 0.05 μ g. may be detected, has been described.²⁵ The reagent, which gives a yellow precipitate with lithium, is a solution of 2 g. of potassium periodate in 10 ml. of 2N-potassium hydroxide diluted to 50 ml. and to which 3 ml. of 10% aqueous hydrated ferric chloride have been added, the whole being made up to 100 ml. Additional data of the sensitivity of this test, and a discussion of the difficulties encountered in the extraction of lithium chloride from mixed alkali chlorides, with particular reference to the determination of lithium in mineral waters and silicate rocks, have been given by O. Hackl.²⁶ A microtechnique, employing the carbonate test for lithium, enables a few tenths of a mg. to be detected,²⁷ and high selectivity of the test is claimed.

Differences in the solubilities of certain of their salts form the basis of methods for the determination of *rubidium* and *cæsium* when they occur together, though either may be determined satisfactorily, as the perchlorate or chloroplatinate in the absence of the other, or in the presence of sodium and lithium. The separation of rubidium and cæsium by precipitation of the complex chloride $4\text{CsCl} \cdot 4\text{SbCl}_3 \cdot \text{FeCl}_3$ ²⁸ is not wholly satisfactory, since the precipitation of cæsium is incomplete under conditions that avoid coprecipitation of rubidium. Reliable methods for the clean separation of rubidium, or rubidium and cæsium, from potassium have not yet been standardised. The precipitation of rubidium and cæsium as their chlorostannates is fairly satisfactory when little potassium is present, but the precipitation of the triple nitrites, $\text{M}_2\text{NaBi}(\text{NO}_2)_6$, where $\text{M} = \text{Cs}$ or Rb , is usually preferred.²⁹ The application of stannic bromide to the determination of cæsium in the presence of rubidium and potassium has been described;³⁰ from a solution of the bromides Cs_2SnBr_6 is thrown out by an alcoholic solution of stannic bromide.

Standard chemical methods for the determination of *potassium* are numerous and include precipitation (a) as the chloroplatinate followed by reduction and weighing of the platinum (the method has wide applicability since many of the commonly occurring anions and cations do not interfere); (b) as the perchlorate in butyl- or ethyl-alcoholic solution; (c) by sodium cobaltinitrite. During recent years the use of the cobaltinitrite complex has been investigated³¹ and considerably extended. For the determination

²³ J. Bardet, A. Tchakirian, and R. Lagrange, *Compt. rend.*, 1937, **204**, 443.

²⁴ M. H. Brown and J. H. Reedy, *Ind. Eng. Chem. (Anal.)*, 1930, **2**, 304.

²⁵ O. Procke and R. Uzel, *Mikrochim. Acta*, 1938, **3**, 105.

²⁶ *Z. anal. Chem.*, 1939, **118**, 1.

²⁷ E. R. Caley and A. L. Baker, jun., *Ind. Eng. Chem. (Anal.)*, 1939, **11**, 101.

²⁸ F. Godeffroy, *Ber.*, 1874, **7**, 374; W. Strecker and F. O. Diaz, *Z. anal. Chem.*, 1925/6, **67**, 321; L. Moser and E. Ritschel, *ibid.*, 1927, **70**, 184.

²⁹ W. C. Ball, *J.*, 1909, **95**, 2126; W. C. Ball and H. H. Abram, *J.*, 1913, **103**, 2110, 2130.

³⁰ R. V. Feldman, *J. Appl. Chem. Russia*, 1938, **11**, 1017.

³¹ L. V. Wilcox, *Ind. Eng. Chem. (Anal.)*, 1937, **9**, 136; A. Kawe, *Z. anal. Chem.*, 1939, **115**, 385.

of minute amounts of potassium, I. A. Kaye³² recommends dissolving the precipitate in excess of ceric sulphate, addition of excess potassium iodide solution and titration of the liberated iodine with thiosulphate. For 0.036—0.120 mg. of potassium the average error was +0.5%. Zinc cobaltinitrite has been prepared as a precipitant³³ and is useful when sodium has to be determined after the removal of the potassium. The use of silver cobaltinitrite³⁴ has been recommended as the precipitant for the determination of small amounts of potassium in blood serum;³⁵ the silver is determined titrimetrically, the NO_2' manometrically, and under well-defined conditions the composition of the precipitate is constant. B. Klein and M. Jacobi³⁶ prefer to titrate the NO_2' in the potassium silver cobaltinitrite with ceric sulphate in the presence of ferroin (*o*-phenanthroline-ferrous complex), the error being 2% on 0.1—0.2 mg. of potassium. J. E. Harris³⁷ states that by a modified silver cobaltinitrite method a precipitate is obtained in which the NO_2'/K ratio is constant.

As in the determination of rubidium and caesium, triple nitrites may be used for the rapid determination of potassium. Results obtained gravimetrically by the precipitation of $\text{K}_2\text{CuPb}(\text{NO}_2)_6$ ³⁸ differed by only 0.2—0.4% from those given by the perchlorate method.

H. H. Willard and A. J. Boyle³⁹ have reported an interesting method for the separation and determination of potassium by precipitation as periodate from nitrate solution. The potassium may, in this way, be separated from calcium, zinc, magnesium, aluminium, sodium (70 times the amount of potassium), lithium, nickel, and cobalt. The method is rapid, and accurate for not less than 4 mg. of potassium.

The use of organic reagents as precipitants for potassium continues to grow. I. M. Kolthoff and G. H. Bendix⁴⁰ have examined the gravimetric and volumetric methods for the determination of macro- and micro-quantities of potassium as the salt of hexanitrodiphenylamine (dipicrylamine), *i.e.*, $\text{NH}[\text{C}_6\text{H}_2(\text{NO}_2)_3]_2$. The potassium is precipitated from neutral or alkaline solution by the magnesium or sodium salt of the precipitant, ammonium salts being absent. If the sodium present is more than 80 times that of the potassium, a preliminary separation by the cobaltinitrite method is recommended. The use of the magnesium salt of dipicrylamine for the micro-determination of potassium, and a separation of potassium from 100 times its concentration of sodium has also been described by R. Dworzak and H. Ballezo.⁴¹ V. H. Dermer and O. C. Dermer⁴² have determined the solubilities of the potassium and sodium salts of 2-chloro-3-nitrotoluene-

³² *Ind. Eng. Chem. (Anal.)*, 1940, **12**, 310.

³³ J. Adams, M. Hall, and W. F. Bailey, *Ind. Eng. Chem. (Anal.)*, 1935, **7**, 310.

³⁴ See, *e.g.*, R. J. Robinson and G. L. Putnam, *ibid.*, 1936, **8**, 211; A. S. Ismail and H. F. Harwood, *Analyst*, 1937, **62**, 443.

³⁵ T. E. Weichselbaum, M. Somogy, and H. A. Rusk, *J. Biol. Chem.*, 1940, **132**, 343.

³⁶ *Ind. Eng. Chem. (Anal.)*, 1940, **12**, 687. ³⁷ *J. Biol. Chem.*, 1940, **136**, 619.

³⁸ V. M. Tichomarov and S. N. Cholmogorov, *Zavod. Lab.*, 1938, **7**, 33.

³⁹ *Ind. Eng. Chem. (Anal.)*, 1941, **13**, 137.

⁴⁰ *Ibid.*, 1939, **11**, 94.

⁴¹ *Mikrochem.*, 1939, **26**, 322.

⁴² *J. Amer. Chem. Soc.*, 1938, **60**, 1.

5-sulphonic acid and related compounds. Only the 2-bromo-compound was found to be as suitable as the chloro-compound. The use of dinitronaphthol-sulphonic acid has also been examined.⁴³

Recent volumetric methods include the determination of potassium by precipitation of $K_3PO_4 \cdot 12MoO_3$ by the addition of phosphomolybdic acid, filtration, dissolution of the precipitate in standard potassium hydroxide solution, and titration of the excess.⁴⁴ The determination has also been made by evaporation of the neutral solution with excess of calcium ferrocyanide, extraction with aqueous-alcoholic calcium chloride solution, dissolution of the precipitate in dilute sulphuric acid solution, and titration with 0.1N-potassium permanganate.⁴⁵

B. Physical Methods.

1. *Colorimetric.*—Since details of numerous methods are to be found in Snells "Colorimetric Methods of Analysis,"⁴⁶ in this account the more recent developments will be given emphasis. Methods for the determination of *potassium* include the use of the chloroplatinate, the cobaltinitrite, and the picrate. The chloroplatinate may be dissolved in water, and on the addition of potassium iodide a red colour is produced by only 0.1 p.p.m. The same colour is given by ammonium chloroplatinate, and therefore ammonia and its salts must be absent.⁴⁷ Alternatively, the chloroplatinate may be reduced with stannous chloride; the yellow colour produced is proportional to the platinum and hence to the potassium present.⁴⁸ Methods involving the use of cobaltinitrite rely upon the formation of certain dyes by means of the nitrite in the precipitate.⁴⁹ Precipitation as the picrate is made from alcoholic solution, and the precipitate subsequently dissolved, in the absence of sulphates.⁵⁰ Calcium, magnesium, aluminium, iron, phosphates, and silica do not interfere.

In the investigation of I. M. Kolthoff and G. H. Bendix,⁴⁰ potassium is determined colorimetrically after precipitation by dipicrylamine by dissolution in acetone, dilution with water containing 1 ml. of 0.1N-sodium hydroxide solution/100 ml., and the yellow to orange-red colour determined by a photo-electric colorimeter or Nessler tubes, since Beer's law does not hold. The accuracy and reproducibility of the dipicrylamine colorimetric method has been examined, and thermodynamic data of the amine and its potassium salt evaluated.⁵¹ A modification of the method is reported by E. Amdur,⁵² and its use in the microdetermination of potassium described.⁵³

⁴² E. P. Volotschneva, *J. Appl. Chem. Russia*, 1938, **11**, 369.

⁴⁴ M. I. Ilmenev, *Zavod. Lab.*, 1937, **6**, 1018.

⁴⁵ I. V. Tananaev and E. Dshaparidze, *ibid.*, p. 1079.

⁴⁶ F. D. Snell and C. T. Snell, Chapman & Hall, Ltd., 1936.

⁴⁷ B. J. V. Cuvelier, *Natuurw. Tijds.*, 1932, **14**, 107.

⁴⁸ A. Nemece, *Biochem. Z.*, 1927, **189**, 50.

⁴⁹ See, e.g., C. P. Sideris, *Ind. Eng. Chem. (Anal.)*, 1937, **9**, 145.

⁵⁰ E. R. Caley, *J. Amer. Chem. Soc.*, 1931, **53**, 539; I. N. Antipov-Karataev and A. R. Myasnikova, *Proc. Leningrad Dept. Inst. Fert.*, 1933, **17**, 81.

⁵¹ J. Kielland, *Ber.*, 1938, **71**, 220.

⁵² *Ind. Eng. Chem. (Anal.)*, 1940, **12**, 731.

⁵³ C. R. Harington, *Biochem. J.*, 1941, **35**, 545.

Sodium may be determined as the complex with zinc or magnesium uranyl acetate, by means of the greenish colour of the aqueous solution of the precipitate,⁴⁶ or by conversion of the uranyl radical into the brownish-red uranyl potassium ferrocyanide.^{46, 54} M. C. Darnell and B. S. Walker⁵⁵ prefer to dissolve the zinc sodium uranyl acetate in water and by using a 4400 Å. filter to determine the colour developed by the addition of sodium acetate trihydrate and sulphosalicylic acid. A recent development, with particular reference to the analysis of urine and blood serum, is that of W. C. Woelfel,⁵⁶ in which sodium is determined colorimetrically as uranyl manganese sodium acetate. The precipitate is finally treated with potassium periodate in phosphoric acid solution, and the permanganate colour developed is compared with standards. The method has been examined by E. Leva,⁵⁷ who reports that the presence of potassium causes high results if the ratio K : Na exceeds 1.5; 0.008–0.01 mg. of sodium may be determined with an accuracy of $\pm 8\%$. Sodium may also be determined colorimetrically by (a) precipitation as the pyroantimonate, followed by determination of the antimony as the orange colloidal sulphide; and (b) precipitation as the sodium caesium bismuth nitrite, and subsequent formation of a bright red colour with sulphanilic acid and naphthylamine.⁴⁶

Colorimetric methods for the remaining alkali metals are few. E. S. Burkser and R. V. Feldman⁵⁸ have estimated caesium colorimetrically by first precipitating it with sodium silicomolybdate, centrifuging, and finally adding stannous chloride solution to the washed precipitate suspended in dilute hydrochloric acid. The blue colour which develops is not interfered with by aluminium, potassium, sodium, lithium, iron, magnesium, or sulphate; but lead must be absent.

2. *Spectrographic*.—In 1834 W. H. Fox Talbot observed that by spectroscopic means lithium may be distinguished from strontium; he thereupon began spectrochemical analysis and in particular its application to the alkali metals. G. Kirchhoff and R. Bunsen's work on the metals of this group in 1860, and their discovery of caesium and rubidium, demonstrated early in the history of this field the scope and reliability of spectroscopic methods.

The means of excitation of the spectra, namely, by the arc, spark, or flame, form a convenient mode of classification of spectrographic methods. Arc and spark methods are of general applicability to the detection and determination of about 70 of the 92 elements, and the alkali metals are numbered with these. The flame is of limited applicability, but because of their low excitation potentials the alkali metals are easily determined by this method.

D. T. Ewing, M. F. Wilson, and R. P. Hibbard⁵⁹ employed an *arc* between graphite electrodes for the determination of potassium, lithium, rubidium,

⁵⁴ B. T. Mulwani, *J. Univ. Bombay*, 1940, ii, 8, 128.

⁵⁵ *Ind. Eng. Chem. (Anal.)*, 1940, 12, 242.

⁵⁶ *J. Biol. Chem.*, 1938, 125, 219.

⁵⁷ *Ibid.*, 1940, 132, 487.

⁵⁸ *Zavod. Lab.*, 1938, 7, 166.

⁵⁹ *Ind. Eng. Chem. (Anal.)*, 1937, 9, 410.

cæsium, and other elements in hydrochloric acid solutions of samples of ash; and K. Pfeilsticker⁶⁰ determined alkali metals in the waters of various German rivers by means of an interrupted arc with copper electrodes. The reciprocal effect of alkali metals on the sensitivity of their detection in the arc has been investigated.⁶¹ An arc technique has recently been employed in the determination of sodium in blood serum.⁶² With solutions on graphite, the standard deviation for a single determination is $\pm 3\%$.

An accuracy of 2% in the determination of sodium, and of 3% for potassium present in urine was claimed by O. S. Duffendack,⁶³ who used a *spark* technique similar to that of Twyman and Hitchen. A. Iwamura⁶⁴ has preferred to pass the spark between tablets made of the solution to be examined, syrup, and carbon; cæsium and lithium were determined in this way. The spark technique has also been employed for the determination of sodium in aluminium-silicon alloys.⁶⁵ A. K. Rusanov⁶⁶ made quantitative analyses of solutions for lithium, sodium, and certain other metals by visual examination of the spark spectra and also by photographic photometry with the logarithmic sector on the acetylene flame.

The Ramage and the Lundegårdh technique are both of particular value in the determination of alkali metals in solution by means of *flame* excitation. In the Ramage method a known volume of the solution is absorbed on a standard strip of filter-paper, which is then dried, rolled, and burned in an oxy-coal or oxy-acetylene flame; with the Lundegårdh technique the solution is sprayed in the air supply of an air-acetylene flame. Comparison of the accuracy of the two methods has recently been made by R. L. Mitchell,⁶⁷ who finds that approximately equal accuracy is obtained from quadruplicate determinations by the Ramage and duplicates by the Lundegårdh. Though T. Torok⁶⁸ has preferred the use of chemical reactions which produce a gas to mechanical spraying, the latter is evidently preferred by many workers. Modifications of the Lundegårdh method have been described.^{69, 70} Notable developments and applications of the Ramage technique have been made by W. A. Roach,⁷¹ by F. C. Steward and J. A. Harrison,⁷² who determined rubidium in potatoes, and by N. L. Kent⁷³ (lithium in plant tissue).

Several recent uses of the Lundegårdh method have been reported which include the determination of the alkali metals in soils;⁷⁴ in oranges, beans,

⁶⁰ *Gas- u. Wasserfach*, 1936, **79**, 638.

⁶¹ M. Wada, *J. Soc. Chem. Ind., Japan*, 1938, **41**, 377.

⁶² L. T. Steadman, *J. Biol. Chem.*, 1941, **138**, 603.

⁶³ U.S.P. 1,979,964, March 14, 1932; B.P. 418,298.

⁶⁴ *Bull. Chem. Soc. Japan*, 1938, 1312, 260, 265.

⁶⁵ J. A. C. McClelland and H. K. Whalley, *Spectrochim. Acta*, 1939, **1**, 21.

⁶⁶ *Bull. Acad. Sci. U.R.S.S.*, 1940, **4**, 195.

⁶⁷ *J. Soc. Chem. Ind.*, 1941, **60**, 94.

⁶⁸ *Z. anal. Chem.*, 1939, **116**, 29.

⁶⁹ H. Lundegårdh and T. Philipson, *Agric. Coll. Sweden Ann.*, 1938, **5**, 249.

⁷⁰ M. A. Griggs, R. Johnston, and B. E. Elledge, *Ind. Eng. Chem. (Anal.)*, 1941, **13**, 99.

⁷¹ *Nature*, 1939, **144**, 1047.

⁷² *Ann. Bot.*, 1939, **3** (N.S.), 427.

⁷³ *J. Soc. Chem. Ind.*, 1940, **59**, 148.

⁷⁴ R. L. Mitchell and M. Robertson, *ibid.*, 1936, **55**, 269r.

and blood; ⁷⁰ in tobacco ashes; ⁷⁵ in flue dusts, alloys, precipitates, and miscellaneous chemicals.⁷⁶ The direct determination of some elements, including the alkali metals, from their flame spectra by the use of suitably chosen filters and a photoelectric cell has been described.⁷⁷

The possibility that one element may influence the intensity of the radiation due to another has to be recognised by spectrochemical analysts. The effect of sodium, potassium, and lithium introduced into an acetone vapour-air flame on the intensity of the rubidium emissions has been examined.⁷⁸ Sodium bromide, sodium iodide, and lithium chloride weakened the rubidium line, whilst potassium chloride, sodium fluoride, and sodium sulphate produced a negligible effect. The degree of weakening of the rubidium line was correlated with the heat of formation of the added salt. Calculations of this effect have also been recorded and discussed by S. L. Mandelstam.⁷⁹

4. ALCOHOLS.

The most important substance considered is still ethyl alcohol, the accurate determination of which is rendered the more necessary by the legal requirements, both criminal and fiscal, of many countries. Little change has been made recently in the accepted methods for its estimation, and the main advance has been made in investigations on substances which interfere with its determination, whereby they are either removed from the alcohol before its final determination, or are themselves determined and suitable correction is then applied to the apparent alcoholic concentration. In the latter type of analysis, however, agreement between results obtained by more than one method is desirable.

The Thorpe and Holmes process ¹ is still the most important for *ethyl alcohol*. In this, a partition is made of the sample between brine and light petroleum, the interfering substances being largely dissolved in the latter, while the alcohol is quantitatively retained in the brine, distillation of which yields an aqueous solution of alcohol.

Partly on this account, practically all the methods described are for aqueous solutions, as the number of compounds which affect the accuracy of the determinations is limited by this process to very few. Certain methods, however, are used which do not rely on this. E. G. Kellett ² has modified Agulhon's test by using a 5% solution of concentrated nitric acid in glacial acetic acid for the detection of small amounts of alcohols by their oxidation with 0.1 ml. of 15% aqueous sodium chromate; by comparison of the blue colour produced with appropriate standards it can now be used as a quanti-

⁷⁵ F. G. H. Tate and H. K. Whalley, *Analyst*, 1940, **65**, 587.

⁷⁶ J. A. C. McClelland and H. K. Whalley, *J. Soc. Chem. Ind.*, 1941, **60**, 288t.

⁷⁷ L. Mazza, *Atti X Cong. intern. Chim.*, 1938, III, 438; M. Lundegårdh and K. Boratynski, *Svensk Kem. Tidskr.*, 1938, **50**, 135.

⁷⁸ T. Borovick-Romanova, *Compt. rend. Acad. Sci. U.R.S.S.*, 1938, **21**, 328.

⁷⁹ *Ibid.*, 1939, **22**, 403.

¹ (Sir) T. E. Thorpe and J. Holmes, *J.*, 1903, **83**, 314.

² *Analyst*, 1937, **62**, 728.

tative limit test in the presence of many ethers, esters, and ketones without preliminary treatment, as secondary reactions are suppressed. A pyrolytic technique has been perfected by O. Grane, B. Löfström, and R. Windbladh,³ in which passage of ethyl, *n*- and *iso*-propyl, and the butyl alcohols over aluminium oxide at 300° leads to the quantitative formation of ethylene, propylene, and butylene, respectively, which may be determined by conversion into the corresponding bromides; the method is also applicable to mixtures of alcohols. An unusual physical method for alcohol in aqueous solution is by the determination of the viscosity, an accuracy of 0.05% being claimed by A. Niini.⁴ W. Meyer⁵ considers that the iodine value and melting point of potassium xanthates formed from alcohols can be used only to "judge" the constitution of mixed alcohols.

T. Piccoli⁶ has suggested a new qualitative test for *methyl alcohol* after its concentration in aqueous solution by repeated distillation in the presence of potassium hydroxide. Oxidation by acid permanganate and filtration is followed by the addition of morphine hydrochloride in concentrated sulphuric acid, a red-violet colour being produced. T. von Fellenberg⁷ has found that Denigès's test is still the most satisfactory, whereby the alcohol is oxidised to formaldehyde by acid and permanganate, and the solution is then decolourised by adding oxalic acid. Addition of Schiff's reagent yields a blue-mauve colour with the formaldehyde, and the development of colour by any acetaldehyde present is prevented by the presence of a minimum concentration of acid. He recommends optimum conditions for quantitative practice. It has been improved by W. Preiss,⁸ who advocates photoelectric comparison of the colours, and by C. M. Jephcott,⁹ who discovered that unexpectedly the presence of a certain amount of ethyl alcohol, as well as close control of conditions, are necessary to achieve maximum sensitivity, the limit of detection in solution being 5 p.p.m. In the titrimetric method of W. Ender¹⁰ sodium nitrite and acid are added to the solution and the methyl nitrite evolved is collected in aqueous potassium iodide, the iodine liberated after addition of acid being titrated.

In the quantitative oxidation of solutions of methyl and/or ethyl alcohol by standard potassium dichromate and sulphuric acid, the use of a pressure bottle has been advocated by A. Rapin¹¹ in order to eliminate the troublesome loss of aldehydes that occurs during the usual reflux procedure. E. J. Harris¹² claims that a more dilute (10%) sulphuric acid enables the oxidation of both alcohols to be carried out to the corresponding acids; after titration of the residual dichromate, the formic acid may be oxidised completely by a more concentrated acid dichromate solution. The use of any

³ *Ingeniörs Vetensk. Akad. Handl.*, 1938, No. 147.

⁴ *Suomen Kem.*, 1938, **11**, A, 45.

⁵ *Pharm. Zentr.*, 1937, **78**, 669.

⁶ *Atti Congr. naz. Chim. pura appl.*, 1933, **4**, 773.

⁷ *Proc. 5th Intern. Congr. Tech. Chem. Agric. Ind. Holland*, 1937, **1**, 184.

⁸ *Z. Unters. Lebensm.*, 1939, **77**, 272.

⁹ *Analyst*, 1935, **60**, 558.

¹⁰ *Angew. Chem.*, 1934, **47**, 227.

¹¹ *Helv. Chim. Acta*, 1939, **22**, 72.

¹² *Analyst*, 1937, **62**, 729.

heat is deprecated by L. Semichon and M. Flanzy,¹³ who state that oxidation is complete at 15° if a much more concentrated acid is used, primary alcohols and glycols being converted into the corresponding acids, and secondary alcohols into ketones, without further reaction. Undesirable secondary reactions may also be suppressed by the use of hot dichromate and dilute nitric acid.¹⁴

Less attention has been given to gravimetric methods, though some progress has been made. The dimedon precipitation of formaldehyde has been improved by J. H. Yoe and M. C. Reid,¹⁵ who show that accurate control of the p_H of the solution by buffers, and of the excess of the reagent, are essential for maximum precipitation, while drying the precipitate at 55—65° is recommended, since at 100° there is some loss by sublimation. J. B. Wilson, in his discussion,¹⁶ objects to oxidation methods and, finding M. Flanzy's method¹⁷ too tedious, suggests that the alkyl iodides prepared from mixed methyl and ethyl alcohols, after partial separation by distillation, should be allowed to react with trimethylamine. The tetramethylammonium iodide so formed is insoluble in absolute alcohol and is thus separated from the trimethylethylammonium iodide and weighed.

There has still been but little interest in *n-propyl alcohol*, as it is not frequently in use. One method¹⁸ proposed for its determination is oxidation by distillation with chromic and sulphuric acids, and comparison of the colours developed in the distillate on reaction with vanillin and concentrated hydrochloric acid with similarly prepared standards.

The Boehm-Bodendorff *m*-nitrobenzaldehyde test for *isopropyl* and higher alcohols has been rendered specific for the former by J. A. Miller;¹⁹ exposure of the red-brown ring to ultra-violet light yields an ochre-yellow colour with *isopropyl alcohol*. A Prussian-blue colour is produced by the action of concentrated sulphuric acid on the aqueous alcohol containing a little vanillin;²⁰ although amyl alcohol affords a similar colour, it is seldom present in a Thorpe and Holmes distillate. The mercury sulphate test which, according to C. Stainer and A. Lauwart²¹ and others, yields a yellow precipitate with *isopropyl alcohol*, has been found by S. H. Fleming²² to give negative results with the pure substance. Several other tests depend on its oxidation to acetone; indeed, the preferable methods of estimating it are based on this. For instance, M. Metra, L. Lesage, and F. Descatoire,²³ after oxidising it with bromine water and alkaline hydrogen peroxide, apply a modification of Imbert's reaction with sodium nitroprusside to the distillate in order to determine the acetone so formed.

One colour test for *acetone* in aqueous solution which is more sensitive

¹³ *Compt. rend.*, 1932, **195**, 254.

¹⁴ M. H. Cordebar, *J. Pharm. Chim.*, 1939, **30**, 263.

¹⁵ *Ind. Eng. Chem. (Anal.)*, 1941, **13**, 238.

¹⁶ *J. Assoc. Off. Agric. Chem.*, 1935, **18**, 277.

¹⁷ *Ann. Falsif.*, 1935, **28**, 260.

¹⁸ *Apoth.-Ztg.*, 1938, **53**, 1328, 1339.

²⁰ C. L. M. Brown, *Pharm. J.*, 1934, **133**, 560.

²² *Mendel Bull.*, 1935, **7**, 99.

²¹ *J. Pharm. Belg.*, 1928, **10**, 167.

²³ *Compt. rend.*, 1938, **206**, 1026.

than either the nitroprusside or the *o*-nitrobenzaldehyde method, is A. Ravin's²⁴ application of the Frommer-Emilowicz reaction as used by I. N. Korenman.²⁵ The red colour given with an alcoholic solution of salicylaldehyde in presence of concentrated (40%) aqueous sodium hydroxide makes possible the detection and estimation of 0.005 mg. of acetone. Two of the better known titrimetric methods for determining it have been critically examined by C. O. Houghton,²⁶ who finds that with pure acetone Messinger's iodoform method yields high results (102.5%) while Marasco's oxime reaction leads to low figures (97.1%).

The use of the paraformaldehyde method of R. W. Hoff and J. M. Macoun²⁷ for the removal of acetone from aqueous-alcoholic solutions has been found to lead to the formation of traces of methyl alcohol, a fact which immediately prohibits its use for many purposes. The disadvantage is avoided by precipitation of the acetone as the complex by Denigès's acid mercury sulphate. This, however, entails a loss of alcohol by oxidation. C. R. Hoskins²⁸ finds that this loss is greatly diminished by the addition of a small amount of sodium formate to the solution during the formation of the mercury sulphate complex at about 80°, using a known excess of reagent, and precipitation of the remaining mercury in solution by potassium oxalate before distillation.

Some work has recently been published on the investigation of more complex mixtures of these oxygenated solvents. Two may be mentioned as having introduced novel principles. E. J. Boorman²⁹ determines ethyl alcohol in the presence of methyl and isopropyl alcohols and acetone by the simultaneous quantitative oxidation of methyl alcohol to carbon dioxide and water, of isopropyl alcohol to acetone, and of ethyl alcohol to acetic acid (which is determined), by potassium dichromate and sulphuric acid in the presence of mercury sulphate, the total acetone being retained as a stable mercury chromate complex. G. L. Stahly, O. L. Osburn, and C. H. Werkman³⁰ have analysed mixtures of acetone and ethyl, isopropyl, and butyl alcohols by distillation, after oxidation with potassium dichromate and phosphoric acid, and determination of the acetone in the distillate by a modified Messinger's method and of the acetic and butyric acids by their partition between ether and water under standardised conditions.

Also of interest is the method of S. T. Schicktzan, A. D. Etienne, and W. I. Steele³¹ for the analysis of fusel oil, in which the azeotropes formed by the individual alcohols and carbon tetrachloride are separated by fractional distillation.

5. CARBOHYDRATES.

Since the last Report,¹ although new methods have been suggested to separate mixtures of sugars, analysis has progressed rather by the modification and improvement of existing methods.

²⁴ *J. Biol. Chem.*, 1936, **115**, 511.

²⁵ *J. Appl. Chem. Russia*, 1933, **6**, 1002.

²⁶ *Ind. Eng. Chem. (Anal.)*, 1937, **9**, 167.

²⁷ *Analyst*, 1933, **58**, 749.

²⁸ *Ibid.*, 1937, **62**, 530.

²⁹ *Ibid.*, 1939, **64**, 791.

³⁰ *Ibid.*, 1934, **59**, 319.

³¹ *Ind. Eng. Chem. (Anal.)*, 1939, **11**, 421.

¹ *Ann. Reports*, 1938, **35**, 404.

Pentoses.—An example of a modification in the determination of pentoses is the refluxing of a pentose with acid in the usual way, but in the presence of a suitable high-boiling immiscible solvent, *e.g.*, xylene.² The furfuraldehyde formed is rapidly extracted by the solvent, and colorimetric determination of its concentration enables the total amount of furfuraldehyde, and hence of the pentose, to be calculated. The advantages of this procedure are increased accuracy and elimination of the time-consuming steam-distillation of the classical method.

Mixtures of methylpentoses and many other sugars have been analysed by treating them with periodic acid, the acetaldehyde from methylpentoses and the formic acid from other sugars being determined.³

Hexoses and Disaccharides.—1. *Iodine oxidation*. The oxidation of aldoses to aldonic acids by hypiodite, a familiar method for the estimation of these sugars,⁴ has been used as a basis for the characterisation of carbohydrates.⁵ By treatment at $\sim 40^\circ$ with potassium hypiodite in methyl alcohol, aldoses are converted into aldonic acids, which are precipitated in the cold as the potassium salts in the case of glucose, galactose, and arabinose, or as the crude barium salts after addition of barium iodide in methyl alcohol in the case of other aldoses. These salts are condensed with *o*-phenylenediamine to give benziminazoles, which crystallise readily, have sharp melting points, yield good crystalline derivatives, and are claimed to possess many advantages over osazones for characterising sugars.

A method has been described for the micro-determination of lactose in the presence of monosaccharides.⁶ Lactose is oxidised by alkaline iodine solution to lactobionic acid, which is then hydrolysed with aqueous hydrochloric acid. The resulting galactose is determined by the Hagedorn-Jensen procedure.

2. *Fehling's solution*. Potentiometric methods have been applied to the determination of glucose. H. T. S. Britton and L. Phillips⁷ have shown that, although not so rapid as the orthodox volumetric method of J. H. Lane and L. Eynon,⁸ potentiometric titrations of Fehling's solution with glucose solution are possible. Since low and negative "redox" potentials prevail near the end-point of the titration, there is a tendency for the cuprous oxide to be oxidised, and consequently the use of external indicators, *e.g.*, potassium ferricyanide, in Fehling's titrations must result in inaccuracies. It is confirmed that methylene-blue used internally, as in the Lane and Eynon method, is a suitable indicator.

3. *Ferricyanide solution*. The oxidation of glucose in alkaline solution by potassium ferricyanide, the basis of the method of estimation associated with

² R. E. Reeves and J. Munro, *Ind. Eng. Chem. (Anal.)*, 1940, **12**, 551.

³ B. H. Nicolet and L. A. Shinn, *J. Amer. Chem. Soc.*, 1941, **63**, 1456.

⁴ G. M. Kline and S. F. Acree, *Ind. Eng. Chem. (Anal.)*, 1930, **2**, 413.

⁵ S. Moore and K. P. Link, *J. Biol. Chem.*, 1940, **133**, 293.

⁶ S. M. Strepkov and N. K. Succhorukova, *Biochimia*, 1940, **5**, 140.

⁷ *Analyst*, 1940, **65**, 18.

⁸ *J. Soc. Chem. Ind.*, 1923, **42**, 32r.

the names of H. C. Hagedorn and B. N. Jensen,⁹ has been shown to be more suitable for potentiometric titration than the Fehling's method. H. T. S. Britton and L. Phillips¹⁰ have investigated the changes in oxidation-reduction potential as glucose is progressively added to a solution of potassium ferricyanide and sodium carbonate. The potentials before the oxidation of glucose is complete are higher than in the case of Fehling's solution, and after passing the end-point are more negative. The excellent inflexions obtained in the titration curve give greater accuracy to the titration than in the Fehling method. Methylene-blue is shown to be a serviceable indicator in this case also.

A ferricyanide method, which uses as reagent potassium ferricyanide, sodium carbonate, and disodium hydrogen phosphate solution, has been used by H. C. Becker and D. T. Inglis¹¹ to determine fructose in the presence of glucose and sucrose, reduction taking place at 50°. Glucose has a small but definite reducing action on this reagent, and a correction factor has to be introduced, but sucrose has very little reducing action and does not interfere even in large quantities. With fructose concentration <20% of the sugar mixture, an accuracy of 0.5% is claimed for the method, but the error increases rapidly with decreasing concentrations of fructose. The method is not applicable in the presence of maltose or lactose, since both have a reducing action approximately equivalent to that of glucose.

Potassium ferricyanide and ceric sulphate have been used to determine the reducing properties of *l*-sorbose and fructose.¹²

A rapid method of determining reducing sugars, depending on the photocolorimetric measurement of the decolorisation of a standard solution of potassium ferricyanide under prescribed conditions, and using quantities of sugar up to 1.2 mg., has also been described.¹³

4. *Other methods.* Mixtures containing glucose, fructose, maltose, and lactose have been analysed by F. W. Zerban and L. Sattler.¹⁴ Lactose is estimated separately either by oxidation to mucic acid, or better by removal of the other sugars by fermentation with yeast, and subsequent estimation of the residual lactose by copper reduction. Modified Nijns' and Barfoed's reagents are used to estimate glucose and fructose, and the total reducing sugars are determined by Fehling's reduction. Since, however, the reagents used to determine monosaccharides and fructose are slightly reduced by maltose and lactose, corrections are necessary to ensure satisfactory results. The values obtained in the various estimations are introduced into a set of four progressive algebraic equations, and a series of approximate calculations are made until two successive computations are in close agreement. The results obtained on synthetic mixtures agree well with the quantities taken, except in the case of maltose, which is determined by difference.

The reducing power of various sugars with alkaline copper citrate

⁹ *Biochem. Z.*, 1923, 135, 145.

¹⁰ *Analyst*, 1940, 65, 149.

¹¹ *Ind. Eng. Chem. (Anal.)*, 1939, 11, 145; 1941, 13, 13.

¹² F. K. Broome and W. M. Sandstrom, *ibid.*, p. 234.

¹³ S. A. Morell, *ibid.*, p. 249.

¹⁴ *Ibid.*, 1938, 10, 669.

reagent has been investigated.¹⁵ The highest reducing power was possessed by sugars with OH at C₍₃₎, *trans* to OH at C₍₄₎ and C₍₅₎. Sugars with OH at C₍₃₎ or C₍₄₎ in the *cis*-position had a lower reducing power. The configuration of OH at C₍₂₎ did not affect the reducing power greatly. Disaccharides having the glycosidic linkage at C₍₃₎ had a molecular reducing power less than that of the corresponding monosaccharide, but if the linkage was at C₍₄₎ or C₍₆₎, the reducing power was slightly greater than that of the monosaccharide.

Other methods described include the estimation of glucose and fructose in blood and urine,¹⁶ the blue colour formed by treatment with diphenylamine and hydrochloric acid being used to estimate the latter, the analysis of malt extract by selective fermentation,¹⁷ and the microscopic identification of certain sugars by precipitation from saturated aqueous solution by acetone, ethyl alcohol, acetonitrile, and dioxan.¹⁸

Separation of Sugars.—When esterified with azobenzene-*p*-benzoyl chloride, sugars yield coloured esters, which are readily separated by chromatographic adsorption on pure precipitated silica. This has been suggested as a method of separating glucose and fructose,¹⁹ penta-azobenzene-*p*-benzoyl glucose and the corresponding fructose ester being separated by filtration—through a column of precipitated silica—of the ester mixture dissolved in a mixed solvent. Two dark orange zones are formed, separated by a broad colourless zone containing one narrow orange ring. On elution, the top zone yields almost pure fructose ester, the bottom zone almost pure glucose ester. C. D. Hurd and S. M. Cantor²⁰ have elaborated a procedure by means of which sugars of different classes may be separated from one another, and the relative proportions of each in the original mixture estimated. The sugars are converted by stages into the methyl esters, which are then separated by fractional distillation at pressures below 0.02 mm. of mercury. The physical constants of the ester fractions serve to identify the original sugars, and the relative weights of the isolated esters are claimed to agree with the sugars in the original mixture within a few units %. The method has yielded satisfactory results with a variety of sugars, *e.g.*, xylose, rhamnose, glucose, maltose, lactose, gentiobiose, and sucrose, but is not applicable to fructose.

Starch.—The precipitation of "starch-iodide" has been used to estimate starch in plant material,²¹ and W. Whale has applied the starch-iodide method volumetrically.²² Other methods of estimating starch, including methods of hydrolysis with hydrochloric acid, and with diastase and acid,

¹⁵ H. S. Isbell, W. W. Pigman, and H. L. Frush, *J. Res. Nat. Bur. Stand.*, 1940, **24**, 241.

¹⁶ R. W. Martin, *Z. physiol. Chem.*, 1939, **259**, 62.

¹⁷ R. Gardner, *Analyst*, 1939, **64**, 103.

¹⁸ J. A. Quesne and W. M. Dehn, *Ind. Eng. Chem. (Anal.)*, 1939, **11**, 555; 1940, **12**, 556.

¹⁹ W. S. Reich, *Biochem. J.*, 1939, **33**, 1000.

²⁰ *J. Amer. Chem. Soc.*, 1938, **60**, 2677.

²¹ J. J. Chinoy, *Analyst*, 1938, **63**, 876.

²² *Ibid.*, 1939, **64**, 588.

have been reviewed,²³ and a method of determining starch has been described, based upon the use of the enzyme ptyalin in human saliva to convert solubilised starch into maltose, the latter being estimated by heating with alkaline potassium ferri cyanide solution, and titration with ceric sulphate.²⁴

Raw starch decomposes in hot aqueous alkali to give simple acidic substances, principally formic, acetic, and lactic acids, as well as pyruvic aldehyde. Decomposition proceeds more rapidly with acid-modified starches, indicative of increased aldehydic content, and provides an empirical index of hydrolysis. T. J. Schoch and C. C. Jensen²⁵ have used this property of "alkali lability" to investigate a number of theoretical and practical starch problems. The procedure resembles that employed for the saponification number of a fat: digestion of the starch in a measured volume of standard sodium hydroxide, followed by titration of the unconsumed alkali. The rate of decomposition of the starch—termed the "alkali number"—is expressed as the number of c.c. of 0.1N-sodium hydroxide consumed by 1 g. of starch during digestion in alkali for 1 hour at 100°.

When starches are heated with water, the cloudy suspensions formed gradually become translucent as pasting occurs. W. L. Morgan²⁶ has followed this change at various temperatures by photoelectric means and has obtained characteristic curves for each type of starch. By simple mathematical relations, the curves may be applied to the analysis of mixtures of starches.

6. ESSENTIAL OILS.

Essential oils are aromatic, volatile substances, soluble in alcohol and most organic solvents, and slightly soluble in water. They are obtained by steam-distillation of vegetable products, and in general are liquids, though some are semi-solid at room temperature. In composition, they are often complex and may contain terpenes, alcohols, phenols, esters, aldehydes, and ketones. For instance, lavender oil contains linalool, geraniol, nerol, linalyl acetate, pinene, limonene, traces of cineole and thymol, and a small quantity of sesquiterpenes; and camphor oil contains camphor, terpineol, saffrole, eugenol, cineole, pinene, phellandrene, dipentene, and cadinene. Some oils, however, consist mainly of one ingredient. *e.g.*, bitter almond oil, black mustard oil, and wintergreen oil, which are essentially benzaldehyde, allyl isothiocyanate, and methyl salicylate, respectively. The character of an essential oil may be modified by seasonal variation, and by the method of distillation used in preparing it. This variability of composition complicates analysis, and make difficult the detection of the adulteration of expensive with cheaper oils. In examining essential oils, the expert relies considerably on odour; but to the chemist who is concerned only infrequently with

²³ M. P. Etheridge, *J. Assoc. Off. Agric. Chem.*, 1941, **24**, 113.

²⁴ W. Z. Hassid, R. M. McCready, and R. S. Rosenfels, *Ind. Eng. Chem. (Anal.)*, 1940, **12**, 142.

²⁵ *Ibid.*, p. 531.

²⁶ *Ibid.*, p. 313.

essential-oil analysis, odour can be of value only when there is available an authentic sample of the oil for comparison.

Separation of Essential Oils.—In general, distillation and extraction methods are used to separate essential oils in perfumes, drugs, etc. The distillation may be with boiling water or low-pressure steam, or may take advantage of the fact that, in a vacuum, the volatile fractions of most perfumes are entrained in the vapour of ethylene glycol.¹

Alternatively, an extraction method may be employed.² Steam-distillation and alcoholic extraction methods of determining coumarin in sweet clover have been compared, the coumarin being determined colorimetrically by the colour produced by addition of diazotised *p*-nitroaniline to the extract.³

Analysis.—In identifying and estimating essential oils, both physical and chemical methods are employed. The general characters of the oils extend over a wide range, the specific gravity being in most cases less than 1.000, although several oils are known which are heavier than water. The refractive index varies from 1.432 (rue oil) to 1.605 (cassia oil). Many oils are optically active to polarised light, and the optical rotation is a property of importance in assessing purity. The physical properties mentioned, together with boiling range, melting point, colour, solubility in alcohol, and proportion of non-volatile matter present, serve to identify the oil. On the chemical side, the general methods employed are acetylation or phthalation for the alcoholic constituents, oximation for aldehydic and ketonic groups, and saponification for esters. Adulteration is detected mainly by the interpretation of the results obtained from the various tests.

Physical Methods.—Analytical procedure has been considered for several years by a sub-committee which has made recommendations to the "Standing Committee on Uniformity of Analytical Methods of the Society of Public Analysts" on the methods found most trustworthy in essential-oil examination. The sub-committee has prescribed precise methods and apparatus for determining physical properties and solubilities,⁴ and has considered the determination of cineole in cajuput and eucalyptus oils by measurement of the freezing point of a mixture of the dried oil and *o*-cresol.⁵ A subsequent report extends this method to other cineole-containing oils, in which alcohols, esters, aldehydes, and ketones are present in such quantity as to raise the freezing point of the *o*-cresol compound and so indicate a higher cineole content than is actually present.⁶ In such cases, the committee recommends use of the term "Apparent cineole content by *o*-cresol," a figure which may be of value in detecting adulteration.

¹ T. T. Cocking and G. Middleton, *Pharm. J.*, 1932, **129**, 253; L. W. Raymond, *Perfume and Essential Oil Record*, 1936, **27**, 393; S. Sabetay, *Ann. Chim. anal.*, 1939, **21**, 173.

² H. J. Van Giffen, *Pharm. Weekblad*, 1936, **73**, 641.

³ I. J. Duncan and R. B. Dustman, *Ind. Eng. Chem. (Anal.)*, 1937, **9**, 471.

⁴ *Analyst*, 1927, **52**, 53; 1929, **54**, 335; 1930, **55**, 386.

⁵ *Ibid.*, 1927, **52**, 276.

⁶ *Ibid.*, 1931, **56**, 738.

A large number of essential oils and allied substances fluoresce when exposed to ultra-violet radiation.⁷ The fluorescence observed, although not sufficient to characterise oils as natural or synthetic, was of assistance in the classification of oils as regards their principal constituent, and in the detection of adulterants. D. Van Os and K. Dykstra⁸ have examined essential oils by measurement of the ultra-violet absorption, Lambert-Beer absorption curves being obtained for the range 2000—4000 Å. They have used the extinction coefficients of the main absorption bands to determine the amount of anethole in oil of anise, to detect adulterants of oil of anise (which lower the anethole content), and to estimate this oil in other oils. Carvone in caraway oil, eugenol in clove oil, citral in lemon oil, etc., were also determined. Some oils, however, *e.g.*, cajuput, citronella, eucalyptus, etc., since they give no characteristic absorption, cannot be estimated in this way. The method is of value in detecting those adulterants which modify the shapes of the absorption curves. Details have been given of absorption maxima for colour reactions of various essential oils with the Ehrlich-Müller reagent, which consists of two solutions: 5% *p*-dimethylaminobenzaldehyde in acetic acid, and 10% phosphoric acid in acetic acid.⁹ The use of Raman frequencies in the identification of essential oils, and in the distinction of their isomerides, has been suggested.¹⁰

Chemical methods. The sub-committee, already referred to, has considered in detail the chemical methods of determining the various groups in essential oils. Thus, the determination of the acetylisable, *i.e.*, alcoholic, constituents (by acetylation of the oil with acetic anhydride, followed by separation and saponification of the acetylated compound) has been described.¹¹ In general, acetylation methods are known to give variable results, and to indicate as alcohols, certain non-alcoholic constituents, *e.g.*, aldehydes, amines, phenols, esters, etc., which are acetylated along with the alcohols. L. H. Baldinger,¹² varying the times of both acetylation and saponification, found that although the former may vary within wide limits, yet the latter should be restricted to 45—60 mins. He suggested that resinification or polymerisation of certain constituents is induced by prolonged heating with potassium hydroxide, and that some of the base is used up, leading to erroneous results. The observation of C. E. Redemann and H. J. Lucas¹³ that more rapid hydrolysis of esters results if diethylene glycol is substituted for ethyl alcohol as a solvent for potassium hydroxide, has been verified by R. T. Hall, J. H. Holcomb, and D. B. Griffin,¹⁴ who have applied the method to the analysis of the isomers of menthol.

Modifications of the acetylation method have been proposed, using an

⁷ C. P. Wimmer and M. H. Kennedy, *Perfume and Essential Oil Record*, 1930, **21**, 163.

⁸ *J. Pharm. Chim.*, 1937, [viii], **25**, 437, 485.

⁹ A. Müller, *J. pr. Chem.*, 1938, **151**, 233; 1939, **153**, 77.

¹⁰ L. M. Labaune, *Rev. Marques Parfum. Savon.*, 1936, **14**, 145.

¹¹ *Analyst*, 1928, **53**, 214.

¹² *J. Amer. Pharm. Assoc.*, 1939, **28**, 155.

¹³ *Ind. Eng. Chem. (Anal.)*, 1937, **9**, 521.

¹⁴ *Ibid.*, 1940, **12**, 187.

acetylating mixture of pyridine and acetic anhydride.¹⁵ The authors of the first paper state that, under the prescribed conditions, primary alcohols, primary amines, and phenols are quantitatively acetylated in less than an hour, secondary alcohols almost quantitatively in an hour, whilst tertiary alcohols and aldehydes react only with difficulty. T. W. Brignall¹⁶ replaces the pyridine in the acetylating mixture by a less objectionable solvent—*n*-butyl ether—the boiling point of which (142°) is near that of acetic anhydride (140°). The method described avoids saponification of the separated acetylated compound, a major source of error (the amount of acetic anhydride used in the reaction being measured), and is claimed to be applicable to the analysis of free primary and secondary alcohols in any essential oil.

Phthalation in warm pyridine solution has been used as a method of determining primary and secondary alcohols, which are identified as their acid phthalates.¹⁷

The estimation of aldehydic and ketonic groups by the hydroxylamine hydrochloride method has been recommended by the sub-committee in several reports.¹⁸ The method has also been applied to aldehydic and ketonic perfumed ingredients by S. Sabetay,¹⁹ the reaction being carried out in the cold, except with compounds such as pulegone and camphor, which form oximes only with difficulty, and require heating for an hour in a water-bath at boiling point. V. E. Tischtschenko and M. A. Grechnev²⁰ have also used hydroxylamine hydrochloride to estimate camphor.

The sub-committee²¹ has prescribed precise conditions for the saponification of esters, and has discussed the determination of phenolic constituents of essential oils by absorption in 5% aqueous potassium hydroxide.²² P. A. Rowaan and J. A. Insinger²³ have recommended a procedure for the determination of the eugenol content of essential oils, after comparing sodium hydroxide and potassium hydroxide solutions of varying concentrations as extraction liquids at temperatures of 20–100°. The structure of ascaridole, the pharmacologically active constituent of the anthelmintic chenopodium oil, has been investigated,²⁴ and its determination discussed by the sub-committee.²⁵

The “diene” value is a measure of the extent to which combination takes place between compounds containing systems of double bonds, *e.g.*, terpenes, and maleic anhydride. It is an empirical constant of the same

¹⁵ R. Delaby and S. Sabetay, *Bull. Soc. chim.*, 1935, [v], 2, 1716; M. Freed and A. M. Wynne, *Ind. Eng. Chem. (Anal.)*, 1936, 8, 278.

¹⁶ *Ibid.*, 1941, 13, 166.

¹⁷ Y. R. Naves and S. Sabetay, *Ann. Chim. anal.*, 1937, 19, 285; S. Sabetay, *ibid.*, 1939, 21, 289.

¹⁸ *Analyst*, 1930, 55, 109; 1932, 57, 378, 773; 1934, 59, 105.

¹⁹ *Bull. Soc. chim.*, 1938, [v], 5, 1419.

²⁰ *J. Appl. Chem. Russia*, 1936, 9, 1700.

²¹ *Analyst*, 1937, 62, 541.

²² *Chem. Weekblad*, 1939, 36, 642.

²³ H. J. Paget, *J.*, 1938, 829.

²⁴ *Ibid.*, 1928, 53, 215.

²⁵ *Analyst*, 1936, 61, 179.

type as saponification value, etc., and has been used to investigate the phellandrenes²⁶ and to detect and estimate α -terpinene.²⁷

An interesting method for the determination of the essential oils of white and brown mustards by resolution of the glycosides—which contain the oils—with the enzyme myrosin has been described.²⁸ The sulphate produced by the hydrolysis is determined by precipitation with benzidine and titration of the separated benzidine sulphate.

A new optically active reagent for carbonyl compounds, *l*-menthyl *N*-aminocarbamate, has been described²⁹ which gives crystalline derivatives of sharp melting points and definite specific rotations with numerous carbonyl compounds, and has been used successfully in the resolution of *dl*-camphor.

Adulteration of essential oils is common. Oils, such as bergamot and lavender, may contain artificial esters, but sophistication must obviously be limited to esters of high ester value and slight odour, and which are easily obtainable commercially. In general, adulteration is detected by the interpretation of the results obtained from the various tests. The figure mentioned earlier, "apparent cineole content by *o*-cresol," will often indicate that adulteration has taken place, as, for example, where lavender oil has been sophisticated by addition of linalyl acetate or spike-lavender oil, or where rosemary oil has been adulterated with light camphor-oil fractions. D. C. Garratt³⁰ has applied the furfuraldehyde-aniline acetate colour test to detect adulteration. For example, Japanese oil (from *Mentha arvensis*) contains more furfuraldehyde than the better varieties of peppermint oil (from *Mentha piperita*). This test has proved of value also in detecting light camphor oil in rosemary oil, and clove oil in bay or pimento berry, the adulterants having in both cases a higher furfuraldehyde content. Ethyl phthalate is an adulterant of essential oils (as well as being a fixative in perfumes). Y. R. Naves and S. Sabetay³¹ estimate this material in perfumes and balsams by hydrolysis with anhydrous alcoholic potassium hydroxide to potassium phthalate (insoluble in anhydrous alcohol), which may be weighed direct; if, as for example, in balsams, esters such as benzoate or cinnamate are present which also give insoluble potassium salts, the precipitated potassium salts are dissolved in dilute acetic acid, and the phthalate precipitated from the filtrate as the lead salt.

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H. K. WHALLEY.

²⁶ N. F. Goodway and T. F. West, *J. Soc. Chem. Ind.*, 1938, **57**, 37T; A. J. Birch, *J. Proc. Roy. Soc. N.S.W.*, 1938, **71**, 54.

²⁷ R. M. Gascoigne, *ibid.*, 1940, **74**, 353.

²⁸ R. C. Terry and J. W. Corran, *Analyst*, 1939, **64**, 165.

²⁹ R. B. Woodward, T. P. Kohman, and G. C. Harris, *J. Amer. Chem. Soc.*, 1941, **63**, 120.

³⁰ *Analyst*, 1935, **60**, 369, 595.

³¹ *Bull. Soc. chim.*, 1938, [v], **5**, 102.

RADIOACTIVITY AND SUB-ATOMIC PHENOMENA.

OWING to war conditions it has become increasingly difficult to get a clear picture of the progress of science. Many periodicals have become inaccessible and an ever-growing proportion of the research work is being carried out under the seal of military secrecy. To the Reporter, this seems a suitable time for a general survey of our present knowledge of nuclear processes and of the concepts used in explaining and predicting them. This survey is preceded by a historical introduction which briefly recapitulates the steps in which this knowledge was acquired.

During the last decade our knowledge of the atomic nuclei has enormously increased, with regard both to the number of observed facts and to the degree of understanding of their significance.

The first fundamental step was J. Chadwick's discovery ¹ (1932) of the neutron, a particle with practically the same mass as the proton but without electric charge. The discovery of such a particle did away with the necessity to assume the existence of electrons inside the nucleus (an assumption which caused great theoretical difficulties) in order to explain the fact that the atomic weight A is in general greater than the atomic number Z . Instead, it is now generally believed that the atomic nucleus is composed of Z protons and $A - Z$ neutrons, and this assumption, together with plausible assumptions about the forces acting between these elementary particles, accounts for most of the known properties of nuclei, such as their size, spin, statistics and binding energy.

Neutrons were first observed in the disintegration of beryllium by α -particles, and this process is still one of the most convenient ways of producing them, although much larger intensities can be obtained by means of a cyclotron. In passing through matter, neutrons are not influenced by the shell electrons, and they are not repelled by the electric charge of the nuclei. Each neutron is therefore bound to hit a nucleus eventually, even though it may have to pass through several centimetres of solid matter before this happens. The effectivity of neutrons in causing certain nuclear reactions increases considerably if their energy is reduced, and the study of "slow neutrons" (obtained by passing neutrons through water or paraffin wax) has revealed some exceedingly interesting phenomena,² the interpretation of which led to Bohr's theory of the heavy atomic nuclei (1936).

The next important step, only a few months later, was the successful attempt by J. D. Cockcroft and E. T. S. Walton ³ (1932) to disintegrate nuclei by means of ions which had been accelerated through large electric fields. This "artificial" disintegration is not essentially different from

¹ *Nature*, 1932, **129**, 312; *Proc. Roy. Soc.*, 1932, *A*, **136**, 692.

² See, e.g., E. Amaldi and E. Fermi, *Physical Rev.*, 1936, **50**, 899.

³ *Proc. Roy. Soc.*, 1932, *A*, **137**, 229.

the disintegration by natural α -particles, discovered by Rutherford in 1919. It gives, however, a much larger number of disintegrations per unit time and thereby makes their study much less laborious. It also permits the use of projectiles other than α -particles (helium nuclei), thus greatly extending this field of research. Thus the discovery of heavy hydrogen (deuterium) was quickly followed by the use of its ion (the deuteron) as a projectile particularly effective in nuclear disintegration. E. O. Lawrence's ingenious invention of a device in which ions are given very high energies by being accelerated many times in a moderate electric field has made its name "cyclotron" a household word in nuclear laboratories. Lawrence's latest installation produces deuterons of 16 MeV (millions electron volts) and helium nuclei ("artificial α -particles") of 32 MeV. Particles of such energies can overcome the electrical repulsion of even the heaviest nuclei. For the disintegration of light elements, the straightforward acceleration of ions by high electric potentials (up to about 3 MV) has still some advantages, such as simpler operation and more uniform particle energy.

The next great step was the discovery of artificial (or induced) radioactivity.⁴ Again, it must be said that there is no fundamental difference between artificial and natural radioactivity. The great number, however, of radioactive isotopes which can be produced by disintegration of stable elements makes it possible to study many aspects of radioactivity much more completely than was possible before. Neutrons, for the reasons given above, have been found particularly effective in producing radioactive substances. Furthermore, new modes of radioactive disintegration were discovered, such as the emission of positrons (positive electrons), the capture of K -electrons and the transition between isomeric nuclear states.

The discovery of nuclear fission is perhaps not of such fundamental importance, but it showed, for the first time, a possible way of utilising nuclear energies on an engineering scale. A detailed discussion of the fission phenomena and of the possibility of nuclear chain reactions was given in this Report for 1939. Further progress in this field is bound to be slow, and little further evidence has been published since.

Radioactivity.

This term may be taken to indicate the spontaneous transformation of one nuclear species into another. The transformation, being a uni-molecular reaction, follows the well-known equation $N = N_0 e^{-\lambda t}$. Instead of the decay constant λ , the half-value period (half-life) $T = 0.693/\lambda$ is generally used to indicate the rate of decay.

The term "spontaneous" involves a certain ambiguity, since, strictly speaking, the decay of an artificially radioactive substance is not spontaneous but a consequence of a preceding nuclear disintegration. In practice, those transformations which follow the impact of a projectile within a very short time are reckoned as part of the disintegration process while those with a

⁴ F. Joliot and Irène Curie, *Nature*, 1934, **133**, 201.

macroscopic half-life are regarded as spontaneous (radioactive) transformations of the nucleus formed in the disintegration process.

α -Radioactivity.—The emission of helium nuclei (α -rays, α -particles) is very common among the natural radioactive elements, but only one α -active isotope has been produced artificially (by bombarding bismuth with fast He ions from a cyclotron) (see the Report for 1940). The theory of α -activity^{4a} was developed in 1929 and has not changed since. It is simply an application of quantum mechanics to the problem of the motion of a helium nucleus under the forces which the residual nucleus exerts upon it. In leaving the nucleus the α -particle, after overcoming the nuclear attraction, is subjected to repulsion in the electrostatic (Coulomb) field of the nucleus. The joint effect of these two forces is that the particle must cross a "potential barrier," and the quantum-mechanical treatment showed that a particle has a finite probability of doing so even if its energy is too small for it to surmount the barrier. The probability for this "tunnel effect" increases rapidly with increasing particle energy, in quantitative agreement with the experimental facts which are summarised in the Geiger-Nuttall relation $\log \lambda = A + B \log E$, which connects the decay constant λ of the substance with the energy E of the α -particles emitted.

α -Radioactivity is observed among the heaviest elements only, samarium being the lightest element that shows it. This can be explained from the trend of the mass defect curve, according to which α -activity becomes energetically possible only above Z = about 50 and the energy of disintegration (and therefore the rate of decay) gets sufficiently high only at considerably higher Z .

β -Radioactivity.—The theory of this phenomenon is far less well established than that of α -decay. The kinetic energy of the β -particles emitted by any particular substance shows a continuous distribution of values between zero and an upper limit which is equal to the energy available. This means that always some energy "disappears," and to account for this the assumption has been made that in addition to the β -particle, a hypothetical uncharged particle—called neutrino—is emitted and escapes unnoticed, thanks to its lack of electric or other interaction with matter. This assumption forms the basis of E. Fermi's theory of β -decay⁵ and of several variants of this theory, such as the one due to E. J. Konopinski and G. U. Uhlenbeck.⁶ For a discussion of these theories and of their connection with the recently discovered meson (a particle, occurring in the cosmic radiation, with a mass intermediate between those of electron and proton) we must refer to the Report for 1939.

Direct attempts to find effects of the neutrinos from strong radioactive sources have so far been unsuccessful.⁷ This does not argue against their

^{4a} E. U. Condon and R. W. Gurney, *Physical Rev.*, 1929, **33**, 127; G. Gamow, *Z. Physik*, 1929, **52**, 510.

⁵ *Z. Physik*, 1934, **88**, 161.

⁶ *Physical Rev.*, 1935, **48**, 7.

⁷ M. E. Nahmias, *Proc. Camb. Phil. Soc.*, 1935, **31**, 99; H. R. Crane, *Physical Rev.*, 1939, **55**, 501.

existence, since their interaction with matter, as predicted by Fermi's theory, is many million times below the range of the most sensitive methods now available. Positive results have been reported⁸ of an attempt to detect the recoil which a β -active nucleus suffers on account of the emission of the neutrino. These experiments are, however, exceedingly difficult and their interpretation is perhaps not absolutely convincing.

It has been suggested⁹ that neutrinos may be responsible for the so-called new stars (novæ). The authors show that, according to Fermi's theory, production of neutrinos on a vast scale must set in at a certain very high temperature, which may be reached at the centre of some stars. The neutrinos escape, taking large amounts of energy with them, and this cooling effect at the centre of the star causes, in the authors' view, a collapse of the star and an enormous flare-up in its outer layers.

The half-life of β -active substances increases with decreasing transformation energy (upper limit of the β -ray spectrum), though less steeply than in the case of α -decay. This dependence (Sargent's rule)¹⁰ follows also from Fermi's theory. There are, however, many substances whose half-life is much longer than Sargent's rule would indicate; in these cases it is believed that the spins of the radioactive nucleus and the daughter nucleus differ by one or more units, causing the transformation to be "forbidden," in analogy to the forbidden transitions between atomic energy levels.

The shape of the β -ray spectrum has been studied for a great number of β -emitters. The interpretation of the results is complicated by the fact that most of the spectra are complex, *i.e.*, that the nucleus in question has two or more alternative ways of decay, which leave the resulting nucleus in different states of excitation. The excitation energy is nearly always within a very short time emitted as γ -radiation. The so-called coincidence method has often been successfully employed in disentangling the sequence of events. It is, for instance, possible to study the spectrum of those β -particles only which coincide with (*i.e.*, are followed within a very short time by) a γ -quantum, detected by a separate counter. By skilfully combining such experiments, it has been possible in some cases to analyse a complex β -ray spectrum into its simple components. The results, however, do not yet permit a decision between the various β -theories.

The β -particles may be negative or positive electrons. The latter are also called positrons, and by contrast the word electron is often used to denote negative electrons only, though sometimes the word negatron is employed for this.

If the term β -decay is to include any process by which a nucleus is transformed into an isobaric nucleus (one with the same mass number but different charge), then the capture of a K -electron¹¹ into the nucleus must be mentioned here. From the point of view of Dirac's hole theory this process is not

⁸ H. R. Crane and J. Halpern, *Physical Rev.*, 1938, **53**, 798; 1939, **56**, 732.

⁹ G. Gamow and M. Schoenberg, *ibid.*, 1941, **59**, 539.

¹⁰ B. W. Sargent, *Proc. Roy. Soc.*, 1933, **A**, **139**, 659.

¹¹ L. W. Alvarez, *Physical Rev.*, 1938, **54**, 486.

fundamentally different from the emission of a positron. The latter process can be regarded as the capture of one of the (infinitely many) electrons in states of negative energy; the hole left through its removal is the positron observed, according to Dirac. The K-capture is a rather curious kind of "radioactivity": no radiation (save the elusive neutrino) is emitted by the nucleus. The shell electrons, however, have to rearrange themselves after the loss of one of their order and X-rays are therefore emitted which betray what has happened.

The existence of only a limited number of isotopes for each element is intimately bound up with the question of β -stability. Regarding nuclei with odd mass number, it has been long known that each mass number occurs only once among the stable elements, with a few exceptions. This is because, of all the possible isobars of a given odd mass number, only one is stable against β -decay. In those few cases where two adjacent isobars are found in Nature (such as ^{187}Os and ^{187}Re) one of the two is probably always unstable, although the decay may be too slow to be detected.

In the case of nuclei with even mass number, pairs and even triplets of isobars frequently occur, but they occupy only even atomic numbers. For instance, the mass number 124 occurs among the isotopes of tin, tellurium and xenon ($Z = 50, 52$, and 54), but the intervening isobars ^{124}Sb and ^{124}I are not found in Nature and have indeed been proved to be β -active.

This marked difference between odd and even mass numbers can be explained by the assumption (which is supported by other facts) that both the protons and the neutrons tend to associate themselves in pairs in the nucleus. For any odd mass number, this tendency can never be completely satisfied, since either a proton or a neutron is always left over. For even mass number, however, there is a difference between odd and even atomic numbers. The latter are strongly bound and stable because all the protons and neutrons are associated in pairs, while in the former one proton and one neutron is left, making the structure less stable.

Isomeric Transitions.

These are transitions from an excited state of exceptionally long half-life to the ground state of the same nucleus. The reason for these long half-lives is a difference of several units between the spins of the two states (which causes the transition to be highly "forbidden") and the absence of any levels in between which might permit a stepwise transition. A fairly extensive discussion of this phenomenon was given in last year's Report.

Nuclear Collisions.

After discussing the spontaneous transformations of nuclei, we now turn to those processes which are provoked by the impact of a nuclear particle upon a nucleus. The particular reaction in which the nucleus A is hit by the particle a , emits the particles $b, c, d \dots$ and is thereby transformed into the nucleus B , is briefly denoted by $A(a, b, c, d \dots)B$. If A and a are given, $B, b, c, d \dots$ must fulfil the condition that the sums of their mass

and charge numbers must be equal to the corresponding sums for A and a . But this is not all: the energy liberated in the process must be positive, or if it is negative (if energy is absorbed) it must not be greater than the total kinetic energy of A and a , referred to their centre of gravity (if A is, as usually, much heavier than a , this is practically the kinetic energy of A).

In most cases it is found that all the possible reactions within the above limitations do actually occur, at least with light elements. With heavier elements the emission of charged particles is less probable and nearly all collisions result in the emission either of one or more neutrons or of γ -rays (or of both). In many cases the energy of the bombarding particle has a strong effect on the yield and on the character of the reaction.

A complete theory of these phenomena, capable of predicting them in detail, is at present entirely out of the question. Such a theory would indeed require the complete mathematical treatment of the motion of a large number of particles, all strongly interacting, a task infinitely more difficult than the corresponding one concerned with the motion of the atomic electrons in the Coulomb field of the nucleus, where the mutual interactions of the electrons can be regarded as a mere perturbation. Furthermore, the way in which the force between nuclear particles varies with their distance is still not well known, and doubts have even been raised as to the applicability of quantum mechanics to problems in which distances as small as the nuclear radius are involved.

It was N. Bohr¹² who showed that a comparatively simple phenomenological theory of nuclear collisions can be developed just because of the strong interaction of the particles in the nucleus. Because of it, the energy of the impinging particle becomes rapidly distributed over all the other particles of the nucleus, and the resulting system, the "compound nucleus," remains together until by a chance fluctuation enough energy is concentrated in one particle to enable it to break away from the nucleus. If this is the original particle or one of its kind, we say it has been scattered; if it emerges with less than its original energy, we speak of inelastic scattering. If it is a different particle, we speak of a nuclear disintegration. After the emission of one particle the nucleus may still retain enough energy to emit a second one, and even after this a third one. The compound nucleus may also lose energy by γ -radiation or internal conversion (ejection of an inner shell electron); after this, there may or may not be enough energy left for the emission of a particle, or of further γ -radiation. Finally, for the heaviest nuclei, another process, called nuclear fission, is possible; the nucleus divides itself into two smaller nuclei of roughly equal size.

The important point about it is that these things happen one at a time, and can be regarded separately. The impact of the projectile forms the compound nucleus, a system which is characterised by the number of protons and neutrons in it and by its energy and would have the same properties if it had been formed in a different way. The compound nucleus behaves exactly like a radioactive nucleus with several alternative modes of decay,

¹² *Nature*, 1936, 137, 344, 351.

each with its probability per unit time (decay constant). Its half-life is of the order of 10^{-20} to 10^{-15} sec., very short on a human scale but long compared with the time of about 10^{-22} sec. which a particle with several MeV energy requires to travel its own diameter and which may be regarded as a rough "nuclear time unit." If the compound nucleus emits a particle or a γ -quantum, a new system is thereby created, which again has alternative modes of decay, and so on until a stable nucleus is formed.

In its neglect of details (such as the fate of an individual particle in the compound nucleus) this theory is essentially thermodynamical, and the thermodynamical analogy can indeed be pushed to a considerable extent.¹³ The impact of the projectile can be compared to the impact of a fast molecule upon the surface of a very small liquid droplet. The formation of the compound nucleus corresponds to the condensation of the molecule, whereby the temperature of the droplet is raised, on account both of the heat of condensation and of the kinetic energy of the molecule. The droplet can then lose energy either by the evaporation of one or more molecules or by radiation (analogous to the γ -radiation of the nucleus). In order to picture fission as well one would have to endow the droplet with an electrical charge sufficient to lower its effective surface tension almost to zero.

In pursuing this analogy, one must remember that the number of particles in an atomic nucleus is quite small, vastly smaller than the number of molecules in any ordinary thermodynamical system. Furthermore, the "nuclear temperatures," although of the order of 10^{10} degrees for average excitation, are very low in the sense that only a few of the many degrees of freedom of the nucleus are excited. For these reasons, a nucleus cannot take any arbitrary energy value but has discrete energy levels, like an atom.

There is, however, an important difference between a nucleus and an atom. In an atom the levels come closer and closer together with increasing energy until we reach the ionisation limit, where the spectrum becomes continuous: the atom now accepts any amount of energy and immediately splits up into an ion and a free electron which carries away the excess energy. A nucleus, however, does not immediately emit a particle even if there is enough energy for this, but has to wait until enough energy happens to become concentrated upon one particle. With nuclei the transition to the continuous spectrum is, therefore, gradual: * as the energy is increased, the escape of a particle becomes easier, the energy states get broader, and at sufficiently high excitation they merge into a practically continuous spectrum.

Our experimental knowledge of nuclear energy levels is still very incomplete, but as far as it goes it is in good accord with Bohr's nuclear theory. A good deal of evidence has been accumulated about the lowest levels of the lighter elements, by the accurate study of the energy balance in disintegrations. For instance, bombardment of fluorine with α -particles of 5 MeV energy produces several groups of protons, with energies of 5.2, 4.0, 2.2 and 1.3 MeV. If we assume that the emission of a proton with 5.2

¹³ See, e.g., R. Peierls, "Reports of Progress in Physics," 1941.

* In molecules, a similar gradual transition is known as predissociation.

MeV leaves the resulting nucleus in the ground state (the resulting reaction energy $Q = +1.4$ MeV tallies with that calculated from the packing fractions of the nuclei involved), then the emission of the other protons must leave the nucleus with an excitation energy of 1.4, 3.4 or 4.5 MeV. (In calculating the figures, the recoil energy of the nucleus has been allowed for.) Of course there may be other energy levels in between which are not produced by this particular disintegration, but this appears unlikely for various reasons. In some cases where the same nucleus can be obtained from two different disintegration processes [*e.g.*, ^{10}B (α , H) ^{13}C and ^{12}C (D, H) ^{13}C] the same energy levels have been found to be excited.

As long as only the natural α -particles were available these investigations were restricted to the lightest elements (roughly up to calcium), but the use of artificially accelerated ions should permit their extension to higher atomic numbers. The difficulty arises, however, that with increasing atomic number the emission of neutrons rather than charged particles (which are hampered by the "Gamow barrier") becomes prevalent, and energy measurements on neutrons are laborious and inaccurate.

For high atomic numbers some information comes from the γ -rays of the natural radioactive elements. Their energies have been accurately measured (largely by studying the fast electrons produced by their internal conversion) and level schemes have been deduced. They show that the lowest levels of the heavy elements lie, on the whole, considerably closer together than those of the light elements. This agrees well with the liquid-drop model if one assumes that the lowest excitations correspond to deformation oscillations of the nucleus as a whole; a large drop has slower oscillations, with correspondingly lower quantum energies. Some investigations on the γ -rays of artificial radioactive elements support this general trend but show great irregularity in the locations of the lowest levels, indicating that the analogy with a droplet must not be taken too literally.

Performed and interpreted in a different way, disintegration experiments can also give information on much higher energy states, this time not of the resulting but of the compound nucleus. For instance, bombardment of ^{19}F with protons results, as the first step, in the formation of a ^{20}Ne nucleus with an excitation energy equal to the sum of the kinetic energy of the proton and its binding energy of 12.9 MeV. Only if this happens to fit one of the levels of ^{20}Ne can the compound nucleus be formed, and one would expect the reaction to take place only for certain discrete values of the proton energy.

In fact, however, the reaction occurs for all energies over a considerable range, although the yield shows pronounced maxima and minima. This broadening—to the extent of partial overlapping—of the levels is due to the instability of the corresponding nuclear states. According to quantum mechanics, the half-width Γ of any energy level is connected with its decay constant λ by the relation $\Gamma = \hbar\lambda/\pi$. (The wave function of the unstable state has the character of a damped train of waves, and it is well known that resonance becomes less sharp if the damping is increased.)

As the excitation energy is increased, the escape of particles from the nucleus becomes easier and therefore the levels increase in broadness. At the same time the complexity of motion increases, and therefore the average distance between levels gets smaller and smaller. Both trends are clearly shown in the above-mentioned experiments¹⁴ where the intensity of γ -radiation obtained from fluorine under proton bombardment was measured as a function of the proton energy. At low energies (up to about 1 MeV) the graph shows individual peaks of small but measurable width (a few KeV), and at the highest voltage used (2.2 MV) the levels have nearly merged into a continuous mass. Incidentally these peaks have been found very useful in calibrating the energies of artificially accelerated protons, much in the way that spectral lines are used to calibrate optical spectrographs.

The increase of level density with excitation energy is shown impressively by the fact that the average distance between the lowest levels of neon is a few MeV, whereas at an excitation of about 15 MeV it is only a few ten thousand electron volts, or a hundred times less. The intermediate region cannot be observed, since with decreasing proton energy the repulsive electric field of the nucleus (the "Gamow barrier") becomes a greater and greater obstacle.

No such repulsion exists in the case of neutrons, and the nuclear reactions produced by slow neutrons offer some of the most striking illustrations of the characteristics of nuclear levels, or as it is often called, of nuclear resonance.

Neutrons are slowed down by passage through light elements, in particular hydrogen (or hydrogen compounds). The term is generally taken to include both those neutrons which have lost all their energy and are in thermal equilibrium with the slowing-down medium (called thermal neutrons or C-neutrons) and those of energies up to a few hundred electron volts. It was found by Fermi *et al.* that some elements show enormous absorption for slow neutrons. Among them, the behaviour of lithium and boron (more exactly of ${}^6\text{Li}$ and ${}^{10}\text{B}$) is particularly interesting. The absorption of the neutron leads in both cases to the emission of a fast α -particle; it is easy to detect these α -particles by means of an ionisation chamber and a proportional amplifier, and such a chamber, lined with lithium or boron or filled with boron trifluoride, is a very convenient and sensitive detector of slow neutrons.

Furthermore, from our other experience of the width and spacing of nuclear levels, we can be certain that there is no marked influence of nuclear resonance in elements as light as lithium and boron, if the energy of the neutrons is varied, say, between 0 and 1000 eV. From such a light nucleus it is very easy for the α -particle to escape, and the levels should have a width of much more than 1000 eV. In such a case quantum mechanics predict that the absorption should be inversely proportional to the velocity of the neutrons. This absorption law—often briefly called the $1/v$ -law—is equivalent to the statement that the probability for a boron nucleus to absorb

¹⁴ E. G. Bernet, R. G. Herb, and D. B. Parkinson, *Physical Rev.*, 1938, **54**, 398.

a slow neutron depends only on the density of neutrons in its neighbourhood; for if the velocity of a given stream of neutrons is doubled, their density is obviously halved. It is not possible to visualise the $1/v$ -law by thinking of collisions between small spheres; the de Broglie wave-length of a slow neutron is much larger than the diameter of a nucleus and the process is therefore rather analogous to the absorption of a light quantum by an atom. For the same reason, the fact that the absorption cross-section for slow neutrons is often many hundred or even thousand times larger than the true size of the nucleus does not indicate any contradiction to the generally accepted view that the forces between nuclear particles are practically zero at distances larger than 10^{-12} cm.

In most of the heavier elements, however, the capture of a slow neutron is followed by the emission not of an α -particle but of γ -radiation. The width of the level is therefore only of the order of one eV or less. This figure has been derived from plausible assumptions as to the mechanism of radiation and agrees with the width of those neutron resonances which have been studied.

Such a study is easiest in those cases where the nucleus formed by the capture of the neutron is radioactive. Let us, for instance, consider the case of gold. If gold foils are exposed to a beam of slow neutrons, under boron absorbers of varying thickness, their activity is found to decrease at first rapidly and then more slowly with increasing boron thickness. Analysis of the absorption curves shows that there are roughly two groups of neutrons, with absorption coefficients in boron of about 30 and 3 cm.²/g. The first group has been identified with the thermal neutrons, for instance, from the fact that their absorption in boron depends on the temperature of the slowing-down medium. Since the energy of thermal neutrons (at room temperature) is about 0.025 eV, the neutrons in the other group must be ten times as fast, or their energy 2.5 eV. They are very strongly absorbed in gold and yet the activity they produce is not very strong. We conclude that there are not many of these particular neutrons, and since we can calculate the energy distribution of the slow neutrons in any given slowing-down medium (*e.g.*, water) from a statistical consideration of their collision in the medium, we can estimate that only neutrons within an energy region of about 0.1 eV show this selective absorption in gold.

Similar experiments have been carried out with a number of other elements. In all cases the boron absorption curve shows the presence of thermal neutrons, and nearly always a group of resonance neutrons, of energy characteristic of each element. In some cases there are indications of the presence of more than one group of resonance neutrons. Of course, each element must really have a large number of resonance levels, but only those with the lowest energy are readily detected by these experiments. Cadmium is of particular interest, since it has a resonance level at about 0.1 eV. It is therefore a strong absorber for thermal neutrons and, at the same time, practically transparent for neutrons of 1 eV or more. Cadmium sheets are therefore widely used either to cut out thermal neutrons when they are

not wanted or to study their properties by taking alternate measurements with and without a screen of cadmium.

It may seem that the experimental evidence for these resonance phenomena is somewhat indirect and unconvincing. Actually there are a great many more experiments in their support, most of them carried out with very simple equipment but devised and interpreted with great ingenuity, and the totality of their evidence is very convincing indeed. Furthermore, very direct evidence has been obtained recently by C. P. Baker and R. F. Bacher.¹⁵ These authors virtually produced slow neutron beams of homogeneous velocity by using a modulated neutron source, giving short periodical bursts of neutrons, and by counting only those which arrived with a given delay at the counter, which was placed at some distance from the source. By varying the time of delay, they were able to plot the absorption of boron, cadmium and indium as a function of the neutron energy, and their results agree well with the conclusions from the earlier, indirect evidence.

Nuclear Photo-effect.

This phenomenon is not essentially different from other disintegrations, if we regard the γ -quantum as just another kind of nuclear projectile. Its absorption by the nucleus forms a "compound nucleus," in this case simply the original nucleus with an excitation energy equal to the energy of the γ -quantum. If the energy is sufficient, a particle may be emitted. Only emission of neutrons has so far been observed, and comparatively little is known about this "nuclear photo-effect," on account of the low yield obtainable, except for deuterium and beryllium, where the threshold is abnormally low (2.2 and 1.6 MeV respectively, instead of 6 to 10 MeV as in most elements). Deuterium and beryllium, irradiated with γ -rays from radium or thorium-C, are therefore occasionally used as a neutron source.

Very Light Nuclei.

For nuclei containing only a few particles the statistical considerations of Bohr's nuclear theory are no longer applicable. On the other hand, the mathematical difficulties in the way of a complete treatment are less formidable, and the experimental study of the collisions between the simplest nuclei is our main source of information about the forces acting between nuclear particles. So far, this information agrees fairly well with the predictions of the meson theory of nuclear forces (see this Report for 1939), but this theory moves at the very edge of quantum mechanics, and real progress will probably depend on some revolutionary change in the foundations of quantum theory.

O. R. FRISCH.

¹⁵ *Physical Rev.*, 1941, **59**, 332.

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TABLE OF ABBREVIATIONS EMPLOYED IN THE REFERENCES.

Abbreviated Title.	FULL TITLE.
<i>A.</i>	British Chemical and Physiological Abstracts (Section A).
<i>Acta phytochim.</i>	Acta phytochimica.
<i>Agric. Col. Sweden Ann.</i>	Lantbruks-Högskolans Annaler, Agricultural College of Sweden.
<i>Amer. Inst. Min. Met. Eng.</i>	American Institute of Mining and Metallurgical Engineers Publication.
<i>Amer. J. Med. Sci.</i>	American Journal of Medical Sciences.
<i>Amer. J. Physiol.</i>	American Journal of Physiology.
<i>Anal. Fis. Quím.</i>	Anales de la Sociedad Española de Física y Química.
<i>Analyst</i>	The Analyst.
<i>Angew. Chem.</i>	Angewandte Chemie (formerly Zeitschrift für angewandte Chemie).
<i>Annalen</i>	Justus Liebig's Annalen der Chemie.
<i>Ann. Bot.</i>	Annals of Botany.
<i>Ann. Chim.</i>	Annales de Chimie.
<i>Ann. Chim. anal.</i>	Annales de Chimie analytique et de Chimie appliquée.
<i>Ann. Chim. Phys.</i>	Annales de Chimie et de Physique (now divided).
<i>Ann. Falsif.</i>	Annales des Falsifications.
<i>Ann. Ferment.</i>	Annales des Fermentations.
<i>Ann. Physik</i>	Annalen der Physik.
<i>Ann. Reports</i>	Annual Reports on the Progress of Chemistry.
<i>Ann. Surg.</i>	Annals of Surgery.
<i>Apoth.-Ztg.</i>	Deutsche Apotheker-Zeitung.
<i>Arch. exp. Path. Pharm.</i>	Archiv für experimentelle Pathologie und Pharmakologie.
<i>Arch. ges. Physiol.</i>	(Pflügers) Archiv für die gesamte Physiologie des Menschen und der Tiere.
<i>Arch. Mikrobiol.</i>	Archiv für Mikrobiologie.
<i>Arch. Sci. phys. nat.</i>	Archives des Sciences physiques et naturelles.
<i>Arkiv Kemi, Min. Geol.</i>	Arkiv för Kemi, Mineralogi och Geologi.
<i>Atti Congr. naz. Chim. pura appl.</i>	Atti del Congresso nazionale di Chimica pura ed applicata.
<i>Atti X Cong. intern. Chim.</i>	Atti del X Congresso internazionale di Chimica.
<i>Aust. J. Exp. Biol. Med.</i>	Australian Journal of Experimental Biology and Medicine.
<i>Avh. norske Vidensk.-Akad. Oslo, Mat.-nat. Kl.</i>	Avhandlingar utgitt av det norske Videnskaps-Akademi i Oslo, Matematisk-naturvidenskapelig Klasse.
<i>B.</i>	British Chemical and Physiological Abstracts (Section B).
<i>Ber.</i>	Berichte der deutschen chemischen Gesellschaft.
<i>Biochem. J.</i>	The Biochemical Journal.
<i>Biochem. Z.</i>	Biochemische Zeitschrift.
<i>Biol. Rev.</i>	Biological Reviews.
<i>Bot. Gaz.</i>	Botanical Gazette.
<i>Brit. Dental J.</i>	British Dental Journal.
<i>Brit. J. Exp. Path.</i>	British Journal of Experimental Pathology.
<i>Brit. Med. J.</i>	The British Medical Journal.
<i>Bull. Acad. Sci. U.R.S.S.</i>	Bulletin de l'Académie des Sciences de l'Union des Républiques Soviétiques Socialistes.
<i>Bull. Chem. Soc. Japan</i>	Bulletin of the Chemical Society of Japan.
<i>Bull. Inst. Pin</i>	Bulletin de l'Institut du Pin.
<i>Bull. Soc. chim.</i>	Bulletin de la Société chimique de France.
<i>Bull. Soc. Chim. biol.</i>	Bulletin de la Société de Chimie biologique.
<i>Bull. Soc. franç. Min.</i>	Bulletin de la Société française de Minéralogie.
<i>Canadian J. Res.</i>	Canadian Journal of Research.
<i>Chem. Abstr.</i>	Chemical Abstracts.
<i>Chem. and Ind.</i>	Chemistry and Industry.
<i>Chem. Reviews</i>	Chemical Reviews.
<i>Chem. Weekblad</i>	Chemisch Weekblad.

Abbreviated Title.	FULL TITLE.
<i>Chem. Zentr.</i>	Chemisches Zentralblatt.
<i>Chinese Med. J.</i>	Chinese Medical Journal.
<i>Coll. Czech. Chem. Comm.</i>	Collection of Czechoslovak Chemical Communications.
<i>Compt. rend.</i>	Comptes rendus hebdomadaires des Séances de l'Académie des Sciences.
<i>Compt. rend. Acad. Sci. U.R.S.S.</i>	Comptes rendus de l'Académie des Sciences de l'Union des Républiques Soviétiques Socialistes.
<i>Compt. rend. Lab. Carlsberg</i>	Comptes rendus des Travaux du Laboratoire Carlsberg.
<i>Compt. rend. Soc. Phys. Hist. nat., Genève</i>	Compte rendu des Séances de la Société de Physique et d'Histoire naturelle de Genève (supplement in Arch. Sci. phys. nat., <i>g.v.</i>).
<i>Current Sci.</i>	Current Science.
<i>Edinburgh Med. J.</i>	Edinburgh Medical Journal.
<i>Gas- u. Wasserfach</i>	Gas- und Wasserfach.
<i>Gazzetta</i>	Gazzetta chimica italiana.
<i>Helv. Chim. Acta</i>	Helvetica Chimica Acta.
<i>Helv. Physica Acta</i>	Helvetica Physica Acta.
<i>Hydrochem. Mat.</i>	Hydrochemische Materialien.
<i>Ind. Eng. Chem. (Anal.)</i>	Industrial and Engineering Chemistry : Analytical Edition.
<i>Indian J. Physics</i>	Indian Journal of Physics.
<i>Ingeniörs Vetensk. Akad. Handl.</i>	Ingeniörs Vetenskaps Akademien Handlingar.
<i>J.</i>	Journal of the Chemical Society.
<i>J. Agric. Chem. Soc. Japan</i>	Journal of the Agricultural Chemical Society of Japan.
<i>J. Amer. Chem. Soc.</i>	Journal of the American Chemical Society.
<i>J. Amer. Pharm. Assoc.</i>	Journal of the American Pharmaceutical Association.
<i>J. Annamalai Univ.</i>	Journal of the Annamalai University.
<i>J. Appl. Chem. Russia</i>	Journal of Applied Chemistry, Russia.
<i>J. Appl. Physics</i>	Journal of Applied Physics.
<i>J. Assoc. Off. Agric. Chem.</i>	Journal of the Association of Official Agricultural Chemists.
<i>J. Bact.</i>	Journal of Bacteriology.
<i>J. Biochem. Japan</i>	Journal of Biochemistry, Japan.
<i>J. Biol. Chem.</i>	Journal of Biological Chemistry.
<i>J. Cell. Comp. Physiol.</i>	Journal of Cellular and Comparative Physiology.
<i>J. Chem. Physics</i>	The Journal of Chemical Physics.
<i>J. Chinese Chem. Soc.</i>	Journal of the Chinese Chemical Society.
<i>J. Clin. Invest.</i>	Journal of Clinical Investigation, The.
<i>J. Electrochem. Assoc. Japan</i>	Journal of the Electrochemical Association of Japan.
<i>J. Exp. Med.</i>	Journal of Experimental Medicine.
<i>J. Franklin Inst.</i>	Journal of the Franklin Institute.
<i>J. Gen. Chem. Russia</i>	Journal of General Chemistry (U.S.S.R.) (formerly chemical part of the Journal of the Physical and Chemical Society of Russia).
<i>J. Gen. Physiol.</i>	Journal of General Physiology.
<i>J. Hyg.</i>	Journal of Hygiene.
<i>J. Indian Chem. Soc.</i>	Quarterly Journal of the Indian Chemical Society.
<i>J. Inst. Metals</i>	Journal of the Institute of Metals.
<i>J. Iron Steel Inst.</i>	Journal of the Iron and Steel Institute.
<i>J. Nutrition</i>	Journal of Nutrition.
<i>J. Opt. Soc. Amer.</i>	Journal of the Optical Society of America.
<i>J. Org. Chem.</i>	The Journal of Organic Chemistry.
<i>J. Pharm. Belg.</i>	Journal de Pharmacie de Belgique.
<i>J. Pharm. Chim.</i>	Journal de Pharmacie et de Chimie.
<i>J. Pharm. Soc. Japan</i>	Journal of the Pharmaceutical Society of Japan (Yakugai-kuzasshi).
<i>J. Physical Chem.</i>	The Journal of Physical Chemistry.
<i>J. Phys. Radium</i>	Journal de Physique et le Radium.
<i>J. Physiol.</i>	Journal of Physiology.
<i>J. pr. Chem.</i>	Journal für praktische Chemie.
<i>J. Proc. Austral. Chem. Inst.</i>	Journal and Proceedings of the Australian Chemical Institute.
<i>J. Proc. Roy. Soc. N.S.W.</i>	Journal and Proceedings of the Royal Society of New South Wales.
<i>J. Res. Nat. Bur. Stand.</i>	Journal of Research of the National Bureau of Standards (formerly Bureau of Standards Journal of Research).
<i>J. Roy. Tech. Coll., Glasgow</i>	Journal of the Royal Technical College (Glasgow).

Abbreviated Title.	FULL TITLE.
<i>J. Sci. Instr.</i>	Journal of Scientific Instruments.
<i>J. Soc. Chem. Ind.</i>	Journal of the Society of Chemical Industry.
<i>J. Soc. Chem. Ind., Japan</i>	Journal of the Society of Chemical Industry, Japan.
<i>J. Univ. Bombay</i>	Journal of the University of Bombay.
<i>Keram. Runds.</i>	Keramische Rundschau und Kunst-Keramik.
<i>Klin. Woch.</i>	Klinische Wochenschrift.
<i>Kolloid. Schurn.</i>	Kolloidni Shurnal.
<i>Kolloid-Z.</i>	Kolloid-Zeitschrift.
<i>Lancet</i>	The Lancet.
<i>Mem. Inst. Chem. Ukrain. Acad. Sci.</i>	Memoirs of the Institute of Chemistry, Academy of Sciences of the Ukrainian S.S.R.
<i>Mendel Bull.</i>	Mendel Bulletin.
<i>Mikrochem.</i>	Mikrochemie vereinigt mit Mikrochimica Acta.
<i>Mikrochim. Acta</i>	Mikrochimica Acta.
<i>Min. Mag.</i>	Mineralogical Magazine and Journal of the Mineralogical Society.
<i>Monatsh.</i>	Monatshefte für Chemie und verwandte Teile anderer Wissenschaften.
<i>Naturwiss.</i>	Die Naturwissenschaften.
<i>Natuurw. Tijdschr.</i>	Natuurwetenschappelijk Tijdschrift.
<i>Nuovo Cim.</i>	Nuovo Cimento.
<i>Pharm. Acta Helv.</i>	Pharmaceutisch Acta Helvetica.
<i>Pharm. J.</i>	Pharmaceutical Journal.
<i>Pharm. Weekblad</i>	Pharmaceutisch Weekblad.
<i>Pharm. Zentr.</i>	Pharmaceutische Zentralhalle.
<i>Phil. Mag.</i>	Philosophical Magazine (The London, Edinburgh and Dublin).
<i>Phil. Trans.</i>	Philosophical Transactions of the Royal Society.
<i>Phot. J.</i>	Photographic Journal.
<i>Physical Rev.</i>	Physical Review.
<i>Physikal. Z.</i>	Physikalische Zeitschrift.
<i>Physikal. Z. Sovietunion</i>	Physikalische Zeitschrift der Sowjetunion.
<i>Physiol. Rev.</i>	Physiological Reviews.
<i>Proc. Camb. Phil. Soc.</i>	Proceedings of the Cambridge Philosophical Society.
<i>Proc. Imp. Acad. Tokyo</i>	Proceedings of the Imperial Academy (Tokyo).
<i>Proc. Indian Acad. Sci.</i>	Proceedings of the Indian Academy of Science.
<i>Proc. Leeds Phil. Soc.</i>	Proceedings of the Leeds Philosophical and Literary Society.
<i>Proc. Leningrad Dept. Inst. Fert.</i>	Proceedings of the Leningrad Departmental Institute of Fertilisers.
<i>Proc. Nat. Acad. Sci.</i>	Proceedings of the National Academy of Sciences.
<i>Proc. Physical Soc.</i>	Proceedings of the Physical Society of London.
<i>Proc. Roy. Soc.</i>	Proceedings of the Royal Society.
<i>Proc. Soc. Exp. Biol. Med.</i>	Proceedings of the Society for Experimental Biology and Medicine.
<i>Proc. Twenty-fifth Indian Sci. Congress</i>	Proceedings of the Twenty-fifth Indian Science Congress.
<i>Rec. Trav. chim.</i>	Recueil des Travaux chimiques des Pays-Bas et de la Belgique.
<i>Rev. Marques Parfum. Savon.</i>	Revue des Marques de la Parfumerie et de la Savonnerie.
<i>Rev. Mod. Physics</i>	Reviews of Modern Physics.
<i>Ric. sci.</i>	Ricerca scientifica.
<i>Sci. Papers Inst. Phys. Chem. Res. Tokyo</i>	Scientific Papers of the Institute of Physical and Chemical Research, Tokyo.
<i>Sci. Proc. Roy. Dublin Soc.</i>	Scientific Proceedings of the Royal Dublin Society.
<i>Sci. Rep. Tôhoku Imp. Univ.</i>	Science Reports, Tôhoku Imperial University.
<i>Sitzungsber. Heidelberg. Akad. Wiss. math.-nat. Kl.</i>	Sitzungsberichte der Heidelberger Akademie der Wissenschaften.
<i>Spectrochim. Acta</i>	Spectrochimica Acta.
<i>Suomen Kem.</i>	Suomen Kemistilehti (Acta Chemica Fennica).
<i>Svensk Kem. Tidskr.</i>	Svensk Kemisk Tidskrift.
<i>Tek. Ukeblad</i>	Teknisk Ukeblad.
<i>Tids. Kjemi</i>	Tidskrift for Kjemi og Bergvesen.
<i>Trans. Faraday Soc.</i>	Transactions of the Faraday Society.
<i>Z. anal. Chem.</i>	Zeitschrift für analytische Chemie.
<i>Z. angew. Chem.</i>	Zeitschrift für angewandte Chemie (now Angewandte Chemie).

Abbreviated Title.	FULL TITLE.
<i>Z. anorg. Chem.</i> . . .	Zeitschrift für anorganische und allgemeine Chemie.
<i>Z. Biol.</i> . . .	Zeitschrift für Biologie.
<i>Z. Elektrochem.</i> . . .	Zeitschrift für Elektrochemie (und angewandte physikalische Chemie).
<i>Zentr. Min.</i> . . .	Zentralblatt für Mineralogie, Geologie, und Paläontologie.
<i>Z. Metallk.</i> . . .	Zeitschrift für Metallkunde.
<i>Z. Physik</i> . . .	Zeitschrift für Physik.
<i>Z. physikal. Chem.</i> . . .	Zeitschrift für physikalische Chemie, Stöchiometrie und Verwandtschaftslehre.
<i>Z. physiol. Chem.</i> . . .	Hoppe-Seylers Zeitschrift für physiologische Chemie.
<i>Z. tech. Physik</i> . . .	Zeitschrift für technische Physik.
<i>Zavod. Lab.</i> . . .	Zavodskaja Laboratorija.
<i>Z. Unters. Lebensm.</i> . . .	Zeitschrift für Untersuchung der Lebensmittel.
<i>Z. Vitaminforsch.</i> . . .	Zeitschrift für Vitaminforschung.
<i>Z. wiss. Phot.</i> . . .	Zeitschrift für wissenschaftliche Photographic, Photophysik und Photochemie.

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